Southern Medical Journal

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

Volume 49 Number 1

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THE SECTION ON PEDIATRICS 3

5

10

12

17

24

32

39

86

50

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ANNIVERSARY 1956

JAN. 1956

VOLUME 49 NUMBER 1

Southern Medical Journal

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Entered as second-class matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

CONTENTS

Continued from cover 1

ACUTE MONOCYTIC LEUKEMIA: REPORT OF A CASE TREATED WITH CORTISONE AND 6-MERCAPTOPURINE—Leon W. Powell, Jr., Snowden C. Hall, Jr., and John W. Hooker 54

DEFECTS OF THE CARDIAC SEPTA: DIAGNOSIS AND SURGICAL TREATMENT—Dan G. McNamara and Denton A. Cooley 59

THE REGIONAL PROCTOLOGIC SOCIETY—Vincent T. Young 65

EXTRADURAL HEMATOMA OF THE POSTERIOR FOSSA: WITH REPORT OF A CASE—Irwin Perlmutter, Richard E. Strain, and Rhoda Feinstein 66

CLINICAL OBSERVATIONS ON ALLERGIC SENSITIVITY TO INSULIN—Harvey B. Snyder 70

A NEW THERAPEUTIC APPROACH TO CERTAIN CASES OF ALCOHOLISM—Richard C. Proctor 73

UP TO THE PRESENT

TREATMENT OF HYPERTENSION: PART III. PHARMACODYNAMICS IN THERAPY: PERIPHERALLY ACTING AGENTS—John H. Moyer and Edward W. Dennis 76

SOUTHERN MEDICAL NEWS 85

EDITORIALS 86

Circulatory Dynamics in Atherosclerosis

Questions About Cobalt Therapy in Anemia

Of Interest to Young Physicians of the South

The New Gold Cover

THE HOUSTON MEETING 89

TWENTY-FIVE YEARS AGO 94

DOCTOR—DON'T OVERPAY YOUR TAXES 95

BOOK REVIEWS 97

BOOKS RECEIVED 98

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EDITOR, R. H. KAMPMEIER, M.D.
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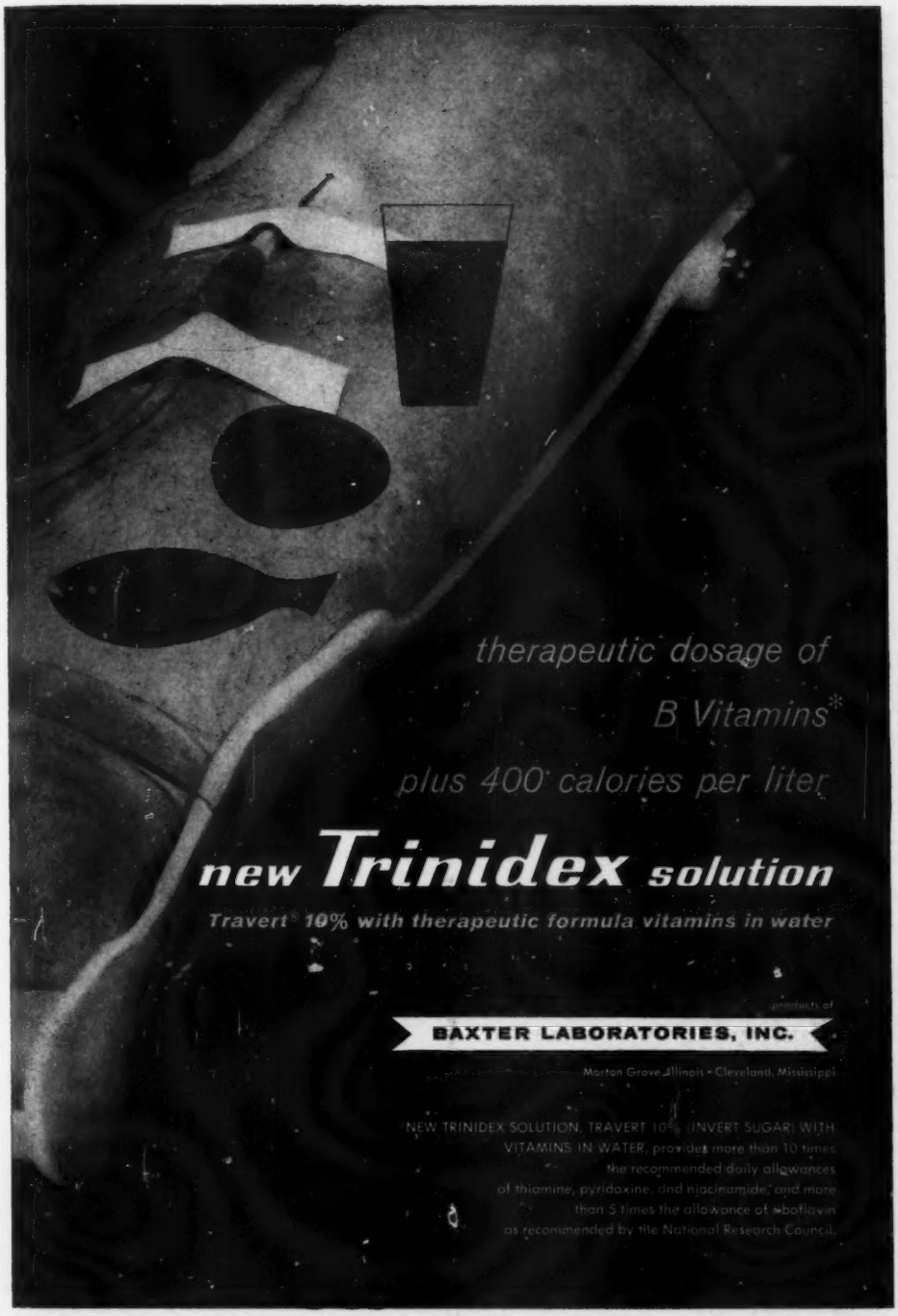
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1. Busse, E.A.: Treatment of Rheumatoid Arthritis by a Combination of Cortisone and Salicylates. Clinical Med. 11:1105 (Nov., 1955).
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3. Coventry, M.D.: Proc. Staff Meet., Mayo Clinic, 29:60 (1954).
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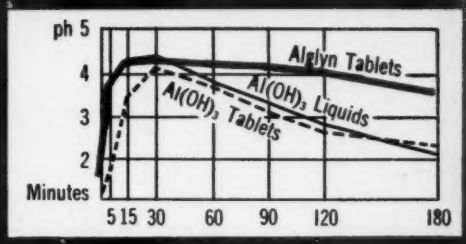

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1. N.N.R., 1956.
2. Hammarlund, E.R. and Rising, L.W.: J. Am. Pharm. Assoc., Scientific Edition, 38:.586, 1949.
3. Rossett, N.E. and Rice, M.L. Jr.: Gastroenterology, 26:.490, 1954.

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1. Sharbor, D.A., and Levitan, M.M.: J.A.M.A. 152:582 (June 20) 1953.
2. Albert, A., and Albert, M.: Texas State J. Med. 50:814 (Dec.) 1954.

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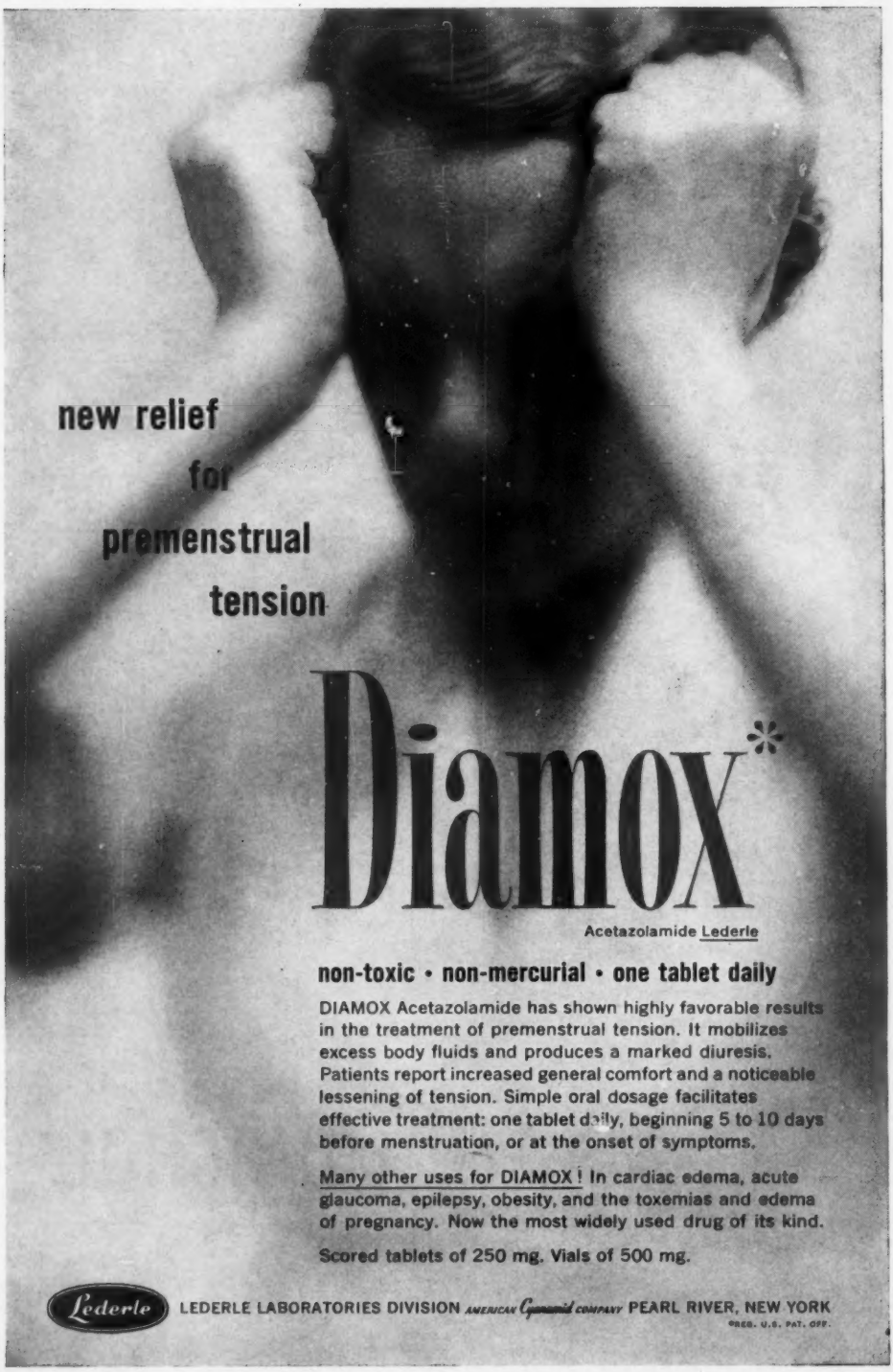
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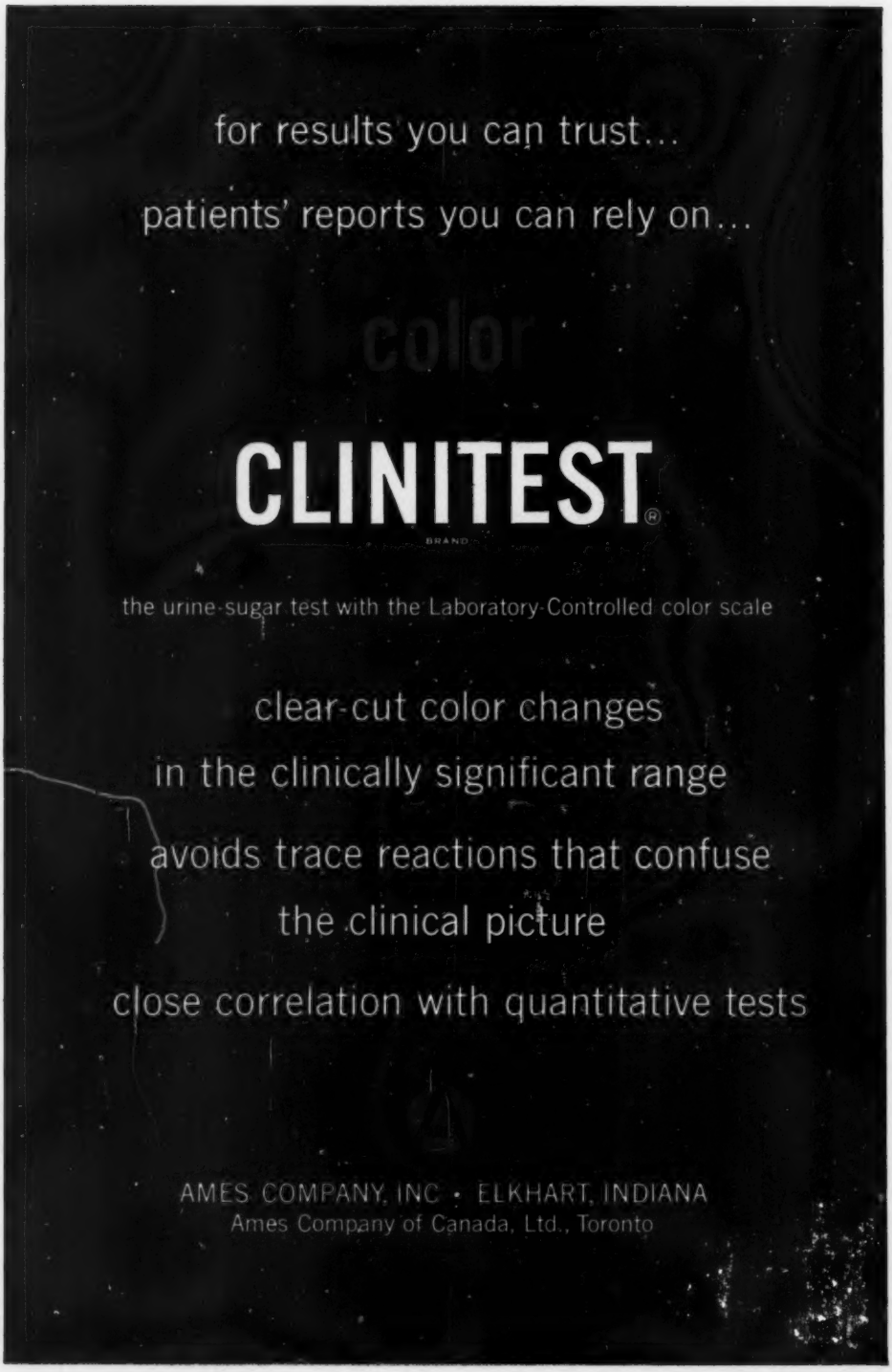
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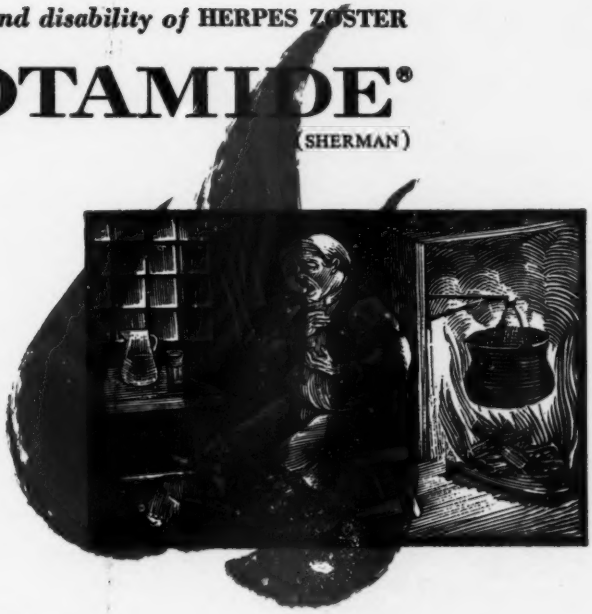

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Combes, F. C. & Canizares, O.: New York St. J. Med. 52:706, 1952; Marsh, W. C.: U. S. Armed Forces M. J. 1:1045, 1950.

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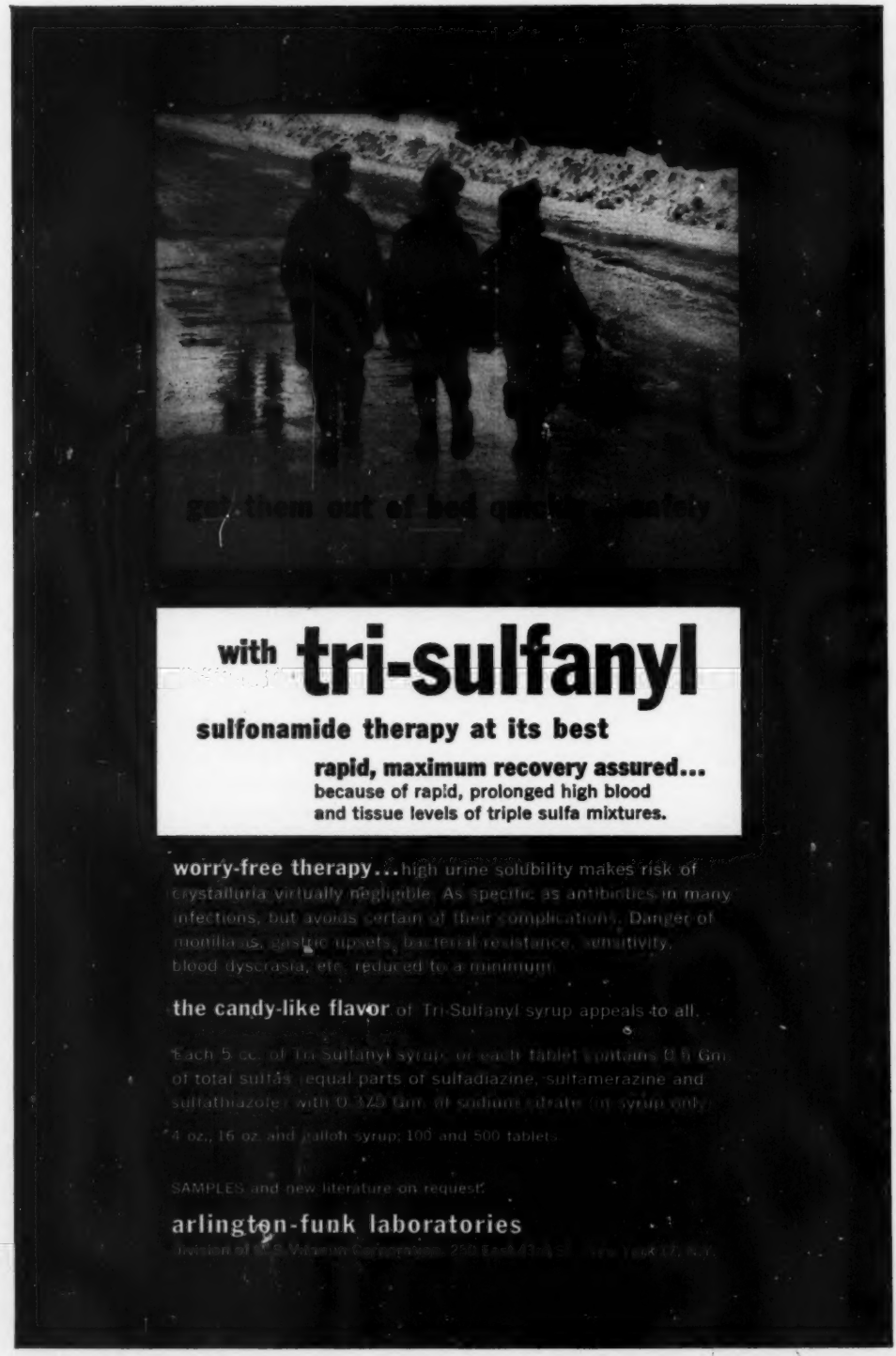
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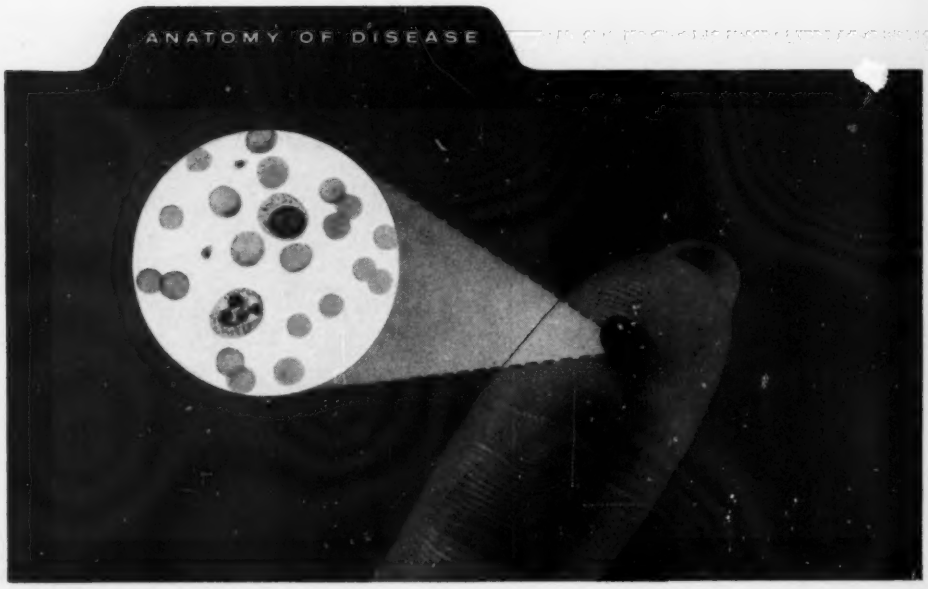

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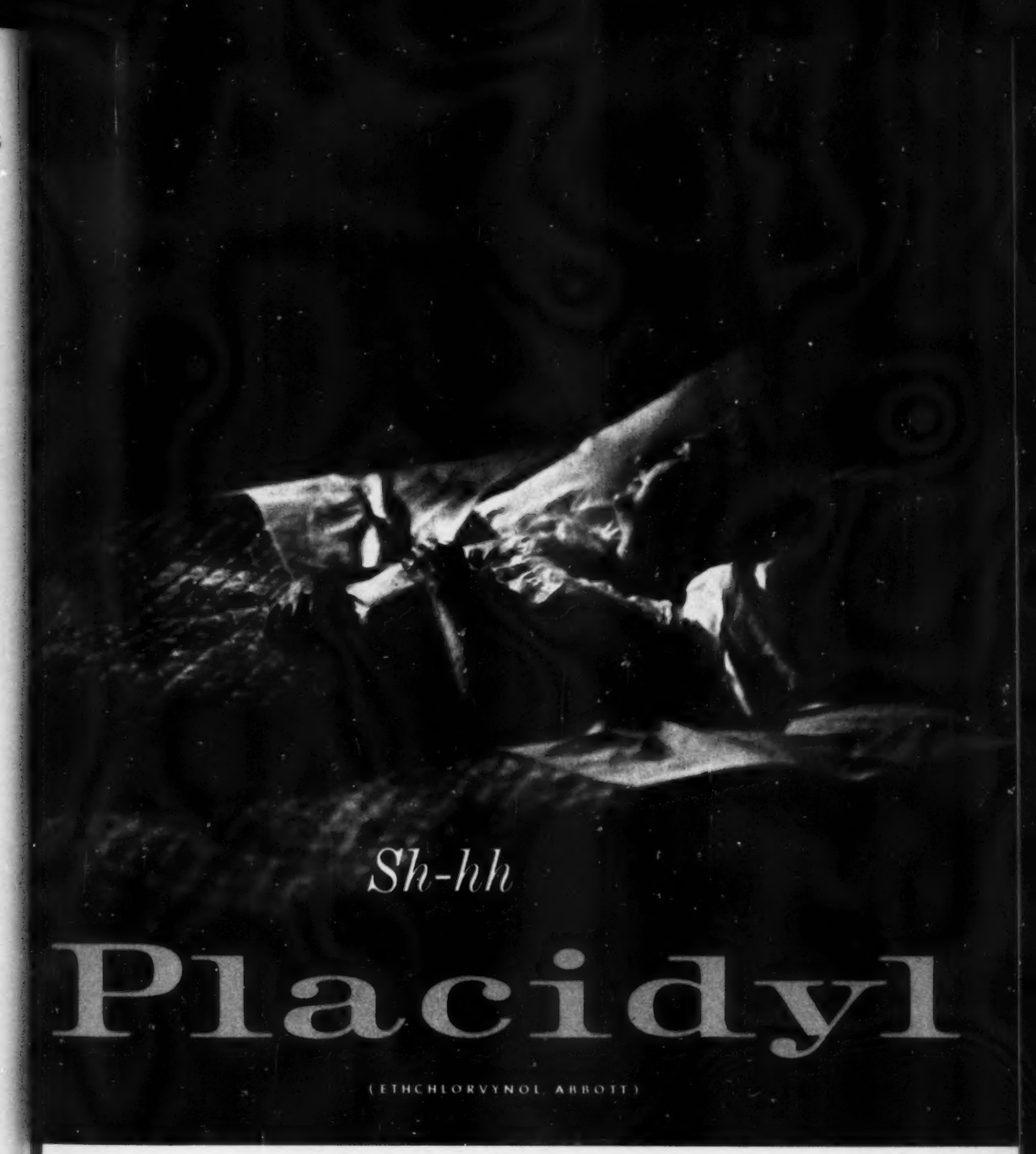

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1. Howell, T.H.; Harth, J.A.P., and Dietrich, M.: Practitioner *173*:172.
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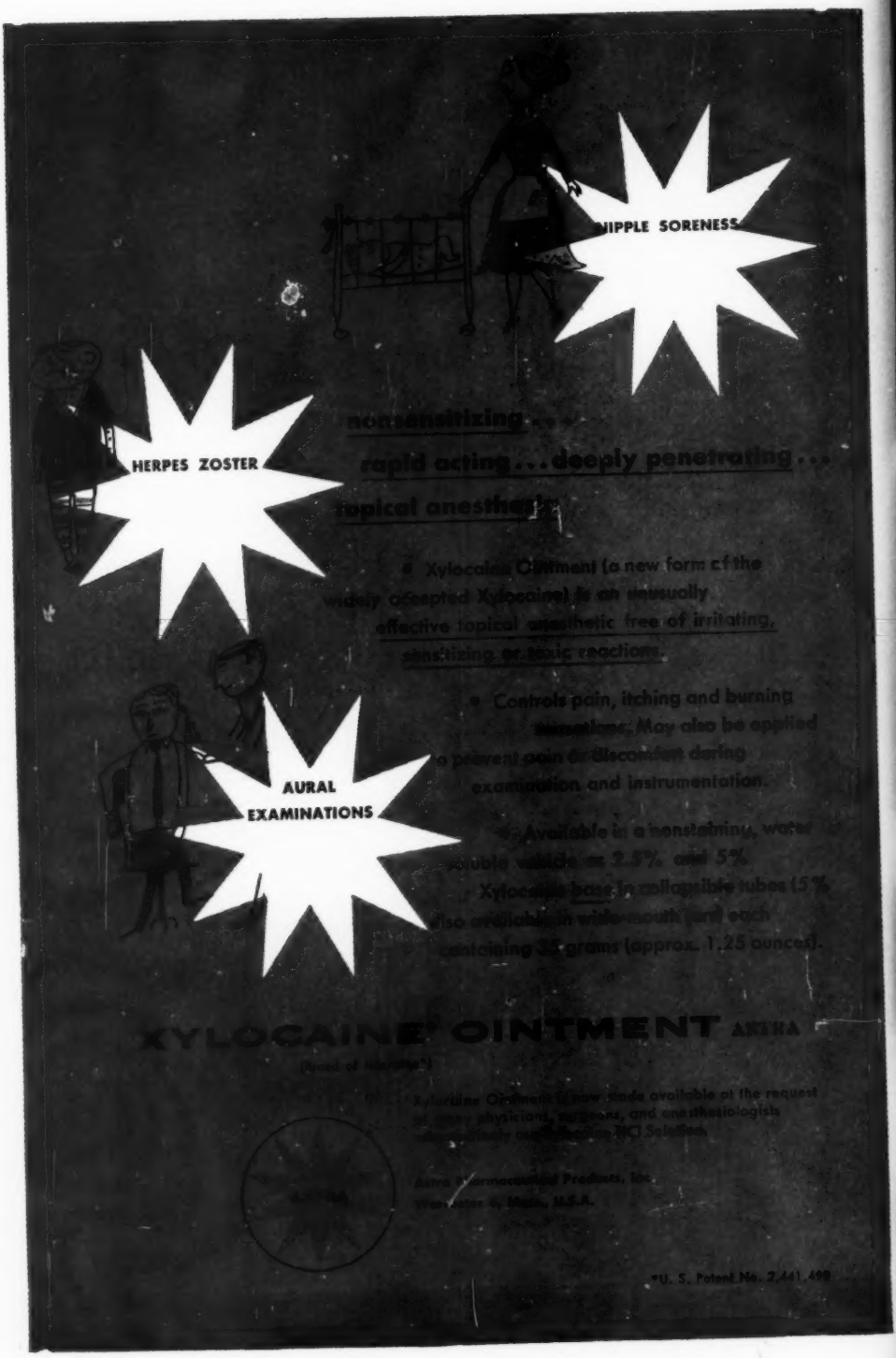
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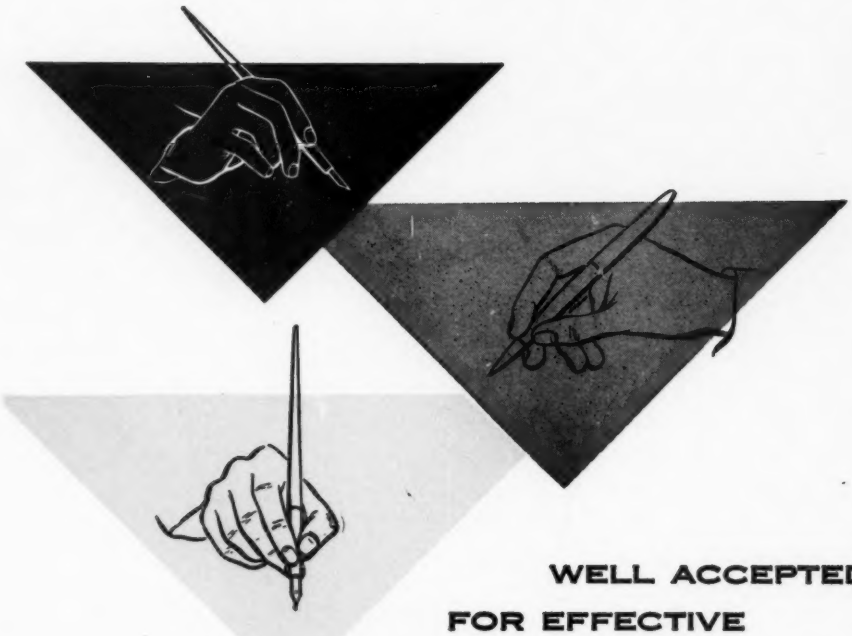

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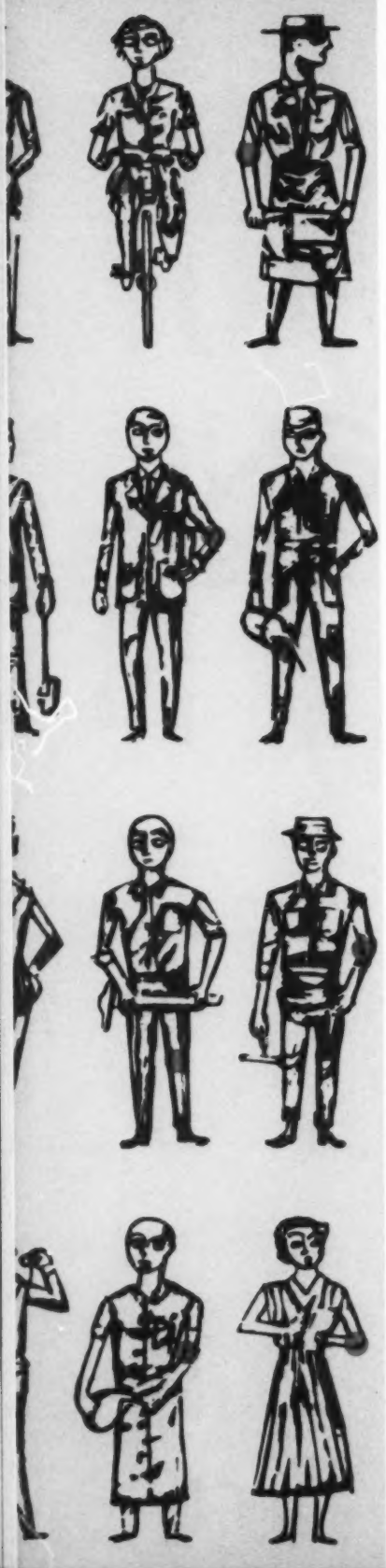

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1. Hyman, S., and Rosenblum, S. H.: Illinois M. J. 104:257, 1953.
2. Piper, C. E., and Nicklas, F. W.: Indust. Med. 23:510, 1954.

†U. S. Pat. 2,628,185

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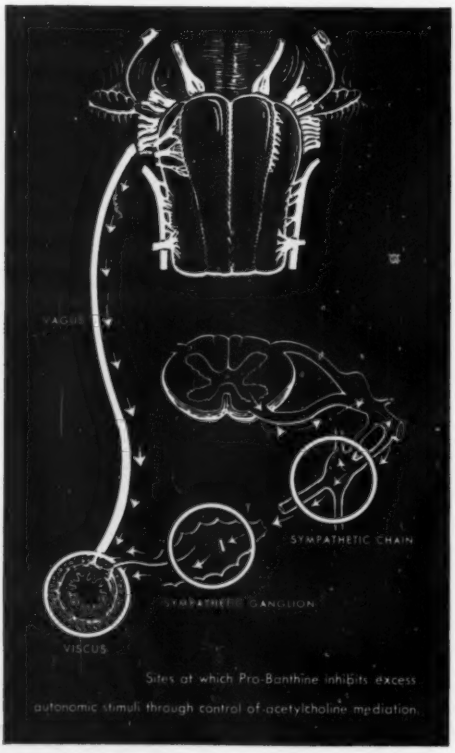

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1. Schwartz I. R.; Lehman, E.; Ostrove, R., and Seibel, J. M.: Gastroenterology *25*:416 (Nov.) 1953.

2. Roback, R. A., and Beal, J. M.: Gastroenterology *25*:24 (Sept.) 1953.

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*Breakey, R. S.; Holt, S. H., and Siegel, D.:
J. Michigan M. Soc. *54*: 805, 1955.

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1. J. Pharm. & Exp. Ther., 89:131
2. J. Urology, 73:487
3. J. Mo. Med. Assoc., 48:135
4. Med. Rec. & Annals, 43:1104

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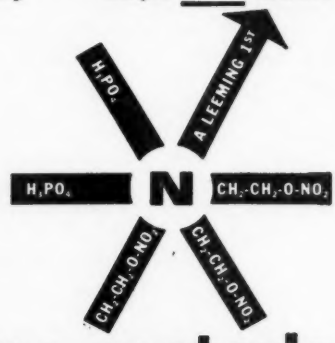

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1. *Siver, Robert H.: Current Medical Digest, Vol. XXI, No. 9, September 1954.*
2. *McGivney, John: Texas State Journal of Medicine, Vol. 51, No. 1, January 1955.*

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Southern Medical Journal

PUBLISHED BY SOUTHERN MEDICAL ASSOCIATION

January 1956

The Range of Loyalty*

FRANCIS P. GAINES,† *Lexington, Va.*

THE HONOR thus accorded me and the scope of opportunity before me duly impressed and humbled but have not inspired me to attempt any kind of technical discussion.

Years ago I heard a story of a small-time farmer in Alabama who had no mode of transportation except a mule and a one-mule buggy. On a given Saturday he went to the county seat and stayed so long that his wife grew alarmed. When he finally got home, by these mutations of feminine logic, her alarm turned into irritation. Trying to defend himself, the husband pleaded: "Well, honey, when I was coming back I run across our preacher and I just had to give him a lift. And, honey, while the preacher was in the buggy with me, that mule couldn't understand a word I said."

For the purposes of this conference, identify me with that mule. I do not understand even the title of the learned documents submitted for your consideration. I strive to find the domains that are common to us as people and citizens, regardless of the assumptive competence by which we make our small bank deposits.

Inevitably such purpose leads to triteness. Prophets and poets chiefly repeat the same elemental, enduring truisms. When I had completed 25 years of service in my present function, the alumni of the University presented me with a new automobile. One of the leaders in this generosity said, "We have started a tradition; every 25 years we give you a new automobile and every 25 years you get up a new speech." This is not one of the new speeches.

Each responsible human being, regardless of mental aspiration or professional commitment, stands in a sense at the center of concentric circles or opportunity and obligation. They evolve from each other into constantly widening dimension. They lead from the simple to the complex, from the tangible to the invisible, from time to eternity. A significant question of our life might be this: "How far in penetrating and commanding these circles goes the range of our loyalty?"

* * *

The first of these circles is that of family, the small and precious circle of heart's affection. They are names we utter repeatedly in private and fervent prayer. These are faces that on lonely and wandering nights we conjure up in appealing vision and beg for a smile. These faces are our inspiration and by mystic mutations of love they become satisfyingly our reward. They are our guiding stars in whatever night.

Somewhere I have read, in footnotes to literature, a story about John Milton. When he was in the early forties he was told that he was going blind. He had three little girls, Anne and Mary and Deborah. The urgency of time was upon him, for he felt that he had much work to do, though we know now that he did his greatest work after he was a blind man. But according to the story he would from time to time lay down his work, snatch a little girl by the arms, stare into her face with intensity that frightened the child and cry in agony, "I must remember! I must remember."

Faces into our night. Faces all through our night. Faces, yet, beyond our night.

I can think of no sweeter promise of the undetermined future than the suggestion of the great Cardinal in the third verse of an immortal song:

So long Thy power had led me, sure it still
Will lead me on;

---

*Read before the First General Session, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

†President, Washington and Lee University, Lexington, Va.

O'er moor and fen, o'er crag and torrent till
The night is gone;
And with the morn those angel *faces* smile,
Which I have loved long since, and lost a while.

* * *

I suppose that the next circle which invites loyalty would be the community—and wise is he who can truly define that engaging word. If episode may be substituted for exposition, I shall turn to memory. Last spring I got in my new automobile and drove many miles to be present at the funeral of an elderly man whom I admired. He was buried about twilight of a lovely day. I walked away from the exercises with a friend who knew this man better than I did, and laboring under strong sentiment I said, "Beautiful hours closed his earthly day."

My friend said, "Yes, his day is closed but his works live after him. There was never a good cause in this community that failed to excite him. Because of his influence, children at this moment have playgrounds in which to romp. Because of him, sick ones of our city have better hospital facilities. Because of him, boys and girls are in college that might not otherwise be there. Because of him, sweeter temples lift their spires to God."

Suddenly, I seemed to hear the children laugh and the church bells ring but—because I am a literature man—I heard most of all my friend's choice of language. He said of this dead one, "Every good cause *excited* him." There was no mere concurrence of the dumb acceptance, no mere willingness to go along with the others in a community project. This dead one was thrilled, was alerted with every nerve tingling, at the sheer prospect of making a happier or nobler community.

Stretch that concept of community far enough to include all mankind and you have a loyalty that ranges and impels in a heavenly radiance.

* * *

Another domain, and a far different domain, challenges loyalty. It could be a summons to life's significant achievement. It could be that at this point we rise to greatness or remain forever earthbound.

Some years ago I was dutifully reading an educational essay. It was called, I think, "The test of an educated man." I do not recall anything dramatic until I got toward the end. Then the author said: "The supreme test of an educated man is his loyalty to an abstract ideal." I recall that the word *abstract* was in italics. To demonstrate his point, the author chose an illustration possibly convincing but most unhappy. He said that any human being, educated or uneducated, who had seen a loved one die of cancer (I have watched a brother and a sister) would remember the agony and the hopelessness and the immeasurable grief, and would probably enlist himself in the fight against cancer. The truly educated man, however, does not need the compulsion of personal experience. He can look at a chart and see a line rising steadily across the squares. It is the death rate of cancer. He has imagination enough to see ten thousand tragedies. He has a loyalty to an abstract ideal of health, or of life's security, and he waits to do what he can in behalf of that ideal threatened by monumental foe.

This business of man's service and sacrifice in behalf of the abstract ideal has lured much of my thinking. There are manifestations without number.

Twice in my life, for example, lawyers have told me a story, the same precise story, though separated by 20 years and 2,000 miles. It is the story of a crime so heinous that it outraged and inflamed public opinion; the story of an honest judge who assigned a young lawyer to defend as best he could the accused; the story of older partners who were horrified that their firm should even be associated with such defense, begging the young lawyer to get out of that case if it took a broken leg or a quick spell of pneumonia; the story of a young lawyer replying, "But don't you see that the more prejudice or mob opinion would settle this case, the more important it is for the accused to have every protection guaranteed by law? I will take the case." I do not have to add that both of these men became superlatively great lawyers. Early in the pathway of their career they had seen a shining light—the ideal of justice.

Of course we tend to generalize freely, but am I not safe in saying that today, in a troubled and terrified age, we need as never before a loyalty to ideals, the consecration

of a soul, those things we must live with or die for.

It was the late summer of 1939—please remember the date. It was a Sunday morning and I was sitting in a little church, looking out upon the everlasting hills. The pastor was making announcements and he said, "The Council of Churches has asked that we pray for peace. I will make the prayer but before I do, I shall ask Dr. Gaines to tell us the world situation—in three minutes."

I walked up. I knew the German army was poised upon the borders of Poland. How could I tell these simple trusting people, living in a vale of peace and plenty, the menace to all their peace and all their plenty?

I had an idea. I said: "I grew up in these wondrous mountains. Just east of me was a county with a funny name. Later I learned the story of that name. It seems that when we began our Revolutionary War, there was a boy in Poland that had everything, family and education and wealth. He heard that in this western world, men were fighting for what they considered freedom. He sailed the long and turbulent leagues of sea and joined the American army. On an October day, while gentle autumnal breezes swayed the hanging moss, he gave up his life just outside Savannah. His name was Casimir Pulaski—and thus the county east of me was named.

"I had for long years a desire to stand by Pulaski's grave and take my hat off. When I finally got to Savannah, I found he did not have a grave; he was buried in the waters, where the river of that fine state, symbol of the local, joins the Atlantic Ocean, symbol of the encompassing.

"But still I seemed to hear the voice of the magnificent boy. He said to me, 'You will remember that it was not my family or my community that was in peril or under attack. I died for an ideal that men call freedom.' Are you ready to do as much for the ideals that give meaning to the common life of all?"

A New Approach for Building A Program for the Section on Pediatrics of the Southern Medical Association*

HARVEY F. GARRISON, M.D., *Jackson, Miss.*

As we come together in this thirty-ninth session of the Section on Pediatrics of the Southern Medical Association we are mindful of the contribution it has made to the profession, of the labors of those who organized it and have served as its officers, of the friendships that have been formed and warmed in its fellowship. Through almost four decades it has been a mighty pioneering force in the South for the medical specialty to which we have dedicated our talents. In fact, it is the pioneer in pediatrics for the South and even had its influence felt in helping to establish the American Academy of Pediatrics and many of the State Pediatric Societies and other organizations for the betterment of infant and child health.

Many of us are affiliated with other professional groups of our specialty—the American Medical Association, whose Section on Pediatrics was created a good many years before the Southern Medical Association was organized; and the American Academy of Pediatrics, which is our youngest pediatric or-

*Chairman's Address, Section on Pediatrics, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

ganization, met in its twenty-fourth session a few weeks ago. But while these organizations have served the profession and our specialty well, meeting as they do, in cities in the North, East and Far West, the expense and time element involved have limited the attendance of our Southern physicians. For instance, at the recent meeting of the Academy in Chicago, only 25 per cent of our members attended, a ratio representative of the attendance from the other Southern states.

The very proximity of the meetings of the Southern Medical Association, held yearly in one of our principal Southern cities, makes it possible for the majority of the membership to attend with little trouble or expense. Tremendous implications lie in this fact—implications that affect the medical proficiency of each physician in the membership, implications that affect public welfare throughout the South, implications that present a challenge to the Section policy makers and program builders. No one can gainsay that the program is the heart of the Section only and the chief justification and cause for its existence. What then of our program? Has it in recent years met the challenge that is ours? Or have we become habituated to a program pattern formulated at the inception of the Section? Our Section, like the Pediatric Section of the American Medical Association, has been conducted on about the same pattern for its entire existence of thirty-nine years.

These questions that I am voicing were raised last year in St. Louis when difficulty with meeting places and accommodations occasioned a good deal of disappointment and dissatisfaction. Handicapped by having meetings in different hospitals about the city, the Section experienced a cutback in attendance, in spite of a good program. The state of affairs was such that the president of the Association invited your chairman to accept the chairmanship of the Section and to attempt to work out some plan that would establish a firm foundation and an entirely new approach for a constructive program for the Section on Pediatrics.

To break away from a fixed pattern is not easy, nor is it always expedient. It is a step which requires serious thought and consideration by the entire Section, for several pertinent questions raise their hands for measured answer. Foremost in our minds is this question: Has the type of program that the Section has had in the past out-lived its usefulness? In surveying the membership, many have expressed the opinion that there should be a decided change in the type of program, with improvement in value and in character. For some to leave the old type program is a rather serious departure from their wonted way. But in our profession we have moved ahead with time: as new drugs, new tools, new therapy have been developed, we likewise have developed new practices. Why then should we be bound to an old pattern of Section procedure when conditions dictate a change?

Another question,—and with this question we attack the root of the whole program problem,—must be considered: Why is it that so few physicians attend regular medical programs? Such is the record not only in pediatrics but in all types of practice. I have observed the attendance because it has been my privilege to attend the Southern Medical Association meetings since shortly after the association was organized 49 years ago. But not trusting the exactness of my cursory observation, I have secured attendance records that glaringly point up the paucity in the number of physicians attending these professional meetings. Is it because we have too many meetings? Conjecture cannot answer that question—the answer must come from performance. In attempting to reach an answer, we must break away from the old order and develop a program that would be so outstanding and constructive that it would not only attract attention of all pediatricians but general practitioners as well. This we have sought to do in this year's Section program. It remains to be seen how well we have succeeded and whether we should follow this new pattern each year.

And right here, I would pause to acknowledge the valuable assistance of those who contributed in building this year's program: our Secretary, Dr. David Greer, Jr.; our Vice-Chairman, Dr. Carroll Pounders; our advisor, Dr. Ralph Bowen; the Executive Secretary of the Southern Medical Association, Mr. V. O. Foster; our President of this Association, Dr. R. L. Sanders; our essayists, eminent teachers in medical colleges, and other outstanding pediatricians.

For almost half a century throughout this territory the Southern Medical Association

has been the real pioneer in advancing good medical knowledge by providing the annual meeting with the necessary facilities, such as scientific exhibits, by investigators, and commercial exhibits and other valuable aids, which keep the profession up-to-date and prepared. The Association is willing to continue to provide these facilities for the advancement of medical knowledge; but it is the responsibility of the Pediatric Section to provide the latest medical thought on pediatrics. We respectfully submit that the most plausible method of meeting this responsibility is in establishing an outstanding intensive three to four day postgraduate course with the cooperation of the Southern medical colleges, which, through their pediatric departments would be responsible for at least 40 to 50 per cent of the annual program.

Certainly it is not unreasonable to anticipate cooperation. The medical colleges in this territory receive practically all of their financial aid from the Southern states. They get the majority of their students from the South. Pediatricians of the Southern states are, in fact, for the most part, former students of these Southern medical schools. Real boosters for their respective schools, they have recommended them to prospective students and have doubtless been responsible for the enrollment of many students. Through such a training program, the schools would keep in closer touch with the pediatrician. Indeed, it would give opportunity for staff members to rub shoulders with their former students, many of whom are now outstanding pediatricians in the South.

A heart warming response has come from letters presenting this idea, written to most of the medical schools in our territory. And it is well known that the pediatricians throughout our states will gladly join with the medical schools in providing a great three to four day intensive postgraduate training program each year.

We have arrived at the time when a new approach is urgent. We have the challenge. We have the personnel. Shall we go forward by utilizing the resources that are ours in this new approach? We have what seems to be a golden opportunity. May we have the vision and the initiative to seize it to the end that our service to humanity may be ever enlarged.

Anorectal Fistulas: Classification and General Principles of Treatment*

B. D. COUGHLIN, M.D., *St. Louis, Mo.*

The author gives his classification of anorectal fistulas and discusses their management.

THE SUBJECT of anorectal fistula continues to be one of the most intriguing problems in proctology. This is due to some confusion regarding a classification and to a surgical approach which many times is inadequate because of a poor knowledge of the anorectal musculature.

The purpose of this paper is to present a classification of those anorectal fistulas which result from an inflammatory process of the anus, the terminal portion of the rectum and/or the contiguous textures. The surgical treatment of some of the complicated fistulas will also be presented.

*Read before the Section on Proctology, Southern Medical Association, Forty-Eighth Annual Meeting, St. Louis, Mo., November 8-11, 1954.

Classification of Anorectal Fistulas

An abscess precedes every fistula of inflammatory origin. The main track of the fistula is the contracted but unobliterated original abscess cavity. Consequently the anatomical

site of the abscess determines the type of resulting fistula. The following classification is hereby presented:

I Subcutaneous anorectal fistula
- a—Complete
- b—Incomplete
  - 1—Internal
  - 2—External

II Submucous anorectal fistula
- a—Complete
- b—Incomplete
  - 1—Internal
  - 2—External
- c—Bilateral

III Intermuscular anorectal fistula
- a—Incomplete
  - 1—Internal

IV Subsphincteric anorectal fistula
- a—Complete
- b—Incomplete
  - 1—Internal
- c—Bilateral or anterior horseshoe

V Ischiorectal fistula
- a—Complete
- b—Incomplete
  - 1—Internal
  - 2—External
- c—Bilateral or posterior horseshoe

VI Pararectal fistula
- a—Complete
- b—Incomplete
  - 1—Internal
- c—Bilateral

Anatomy of Anorectal Musculature

Milligan and Morgan describe the external sphincter as consisting of three layers, a subcutaneous, a superficial and a profundus.

The subcutaneous portion of the external sphincter muscle usually surrounds the entire anal canal at its extremity. It is an annular muscle immediately under the transitional anoderm. The muscle lies in the same vertical plane as the internal sphincter muscle and is separated from the internal sphincter muscle by prominent insertions of the fibroelastic extensions of the conjoined longitudinal muscle. This insertion forms the anal intermuscular septum or the intersphincteric line, an important palpable landmark.

The superficial layer usually arises from the sides of the coccyx and anococcygeal raphe, splitting in an elliptical manner to surround the mid-portion of the anal canal. It covers the circular and longitudinal muscles of the bowel and continues to its insertion in the central perineal tendinous point. The anterior and posterior communicating spaces extend directly above superficialis fibers and below the profundus sphincter fibers.

The profundus layer is the deepest portion, and its fibers usually have an annular arrangement entirely encircling the upper portion of the anal canal. Posteriorly it is closely associated with the puborectal portion of the levator ani muscle and with this muscle it forms the well defined upper border of the anorectal ring. The profundus fibers, only, of the external muscle form the anorectal ring in the anterior half of the anal canal. The puborectalis diverges laterally to surround the vagina in the female and the prostate in male to insert in the lower pubis.

In the surgical treatment of fistula there are two landmarks which should always be recognized by palpation, namely: (1) the division between the subcutaneous external sphincter muscle and the lower border of the internal sphincter muscle which also defines the location of the intermuscular septum, and (2) the anorectal ring in its entire extent.[1]

General Principles of Treatment

The fundamental principle of the surgical treatment of a fistula is to lay open the main track from one end to the other and to seek out all communicating tracks and lay them open. All fistulas may be eradicated this way but the end result depends upon the damage to the anorectal musculature controlling the anal outlet. Although most anorectal fistulas have an internal opening, only in a small percentage of them is the muscular coat of the rectum penetrated by the main track. Consequently the anatomical relationship of the main track to the musculature of the anal outlet determines the type of fistula and its eventual surgical approach.[2] The location of the internal opening is usually the indication of the point where the main track penetrates the bowel wall. This position is usually at the intermuscular septum or Hilton's white line. A high lying internal opening does not always indicate that the main track of the fistula penetrates the wall of the bowel at that point.

Another principle that is important is the area of the surface wound. The surface wound should be at least twice as great as the rest of the wound.

One of the best ways to increase the surface area of a linear wound is to make incisions

through the skin and subcutaneous tissue at right angles to the line of the main incision. The number and position of the secondary incisions or "relieving cuts"[3] depends on individual experience. To serve their purpose properly the surface area should be incised with the least number of secondary incisions. If made at the points of greatest tension along the margin of the main incision the better the result will be. This method saves the loss of a great deal of healthy skin which is sacrificed in the "saucerization" of a fistula. The healing time is much increased and there is less deformity of the anus as the result of excess scar tissue.

Fistula Internal to Bowel Musculature

The Subcutaneous Fistula. The submucous fistula is one which requires definite diagnosis as to the location of the main track in regard to the anorectal musculature. The opening can be found either at the anal margin or through the skin within one-half inch of the margin. A probe introduced into the opening at the anal margin or through the external opening in the skin can be outlined very distinctly by the examining finger. The main track usually run obliquely upward and may run under the primary hemorrhoidal pedicles. Occasionally a bilateral submucous fistula is found on the posterior wall of the rectum with the bilateral extensions ending in a blind cul-de-sac. The median track with an opening in the posterior commissure at Hilton's line forms the upright of a letter T with the bilateral extension.

The Intermuscular Fistula. This rather unusual fistula is one situated between the internal sphincter and the longitudinal muscular coat of the rectum. This type of fistula is never more than one inch long and generally is a complication of a subsphincteric type of fistula. The track follows a straight line cephalad from an opening usually at, or just above Hilton's line to end in a blind cul-de-sac. A probe introduced into the track cannot be distinctly felt and only proceeds not more than one inch in a straight line cephalad. When this type of fistula complicates a subsphincteric or ischiorectal fistula and is not detected at operation the wound fails to heal and pus is consistently discharged until further operation eradicates the intermuscular complication.

Surgical Treatment of Fistulas Internal to the Bowel Musculature. The incision should be made in the direction of the bowel lumen and not in the opposite direction. In a submucous fistula the tissues divided are the mucosa and submucosa. If the track lies under the hemorrhoidal pedicles adequate suturing should be done to prevent hemorrhage. In the intermuscular fistula the tissues divided are the mucosa, submucosal vessels and the internal sphincter musculature. Since the track seldom is greater than one inch in length bleeding is easily controlled. One need not fear any incontinence as a result of dividing the internal sphincter.

Fistulas External to the Bowel Musculature

The pararectal fistula is the end result of an abscess in the pararectal space, bounded internally by the external muscular coat of the rectum and externally by the fascia propria. Whether the abscess is caused by a septic lymphangitis or by a perforation of the rectal wall by a foreign body, the track of the fistula penetrates the rectal wall at a high level. The examining finger can palpate the bulging rectal wall above the levator ani muscle and the mucosa moves freely over the bulge. Early examination and diagnosis can prevent extension into the ischiorectal fossa.

Surgical Treatment. One should never apply the principle of opening the main track into the bowel throughout its entire extent from the external opening to the internal opening.[4] This would result in permanent incontinence because the internal and external sphincters, the attachment of the levator ani muscle to the longitudinal coat of the rectum and the bowel wall as high as the internal opening would be divided. The proper method is to divide the tissues on the outer aspect of the main track to the point where it penetrates the bowel. The incision through the levator ani is made in the direction of the fibers of the muscle and not transversely unless the area of the surface wound demands it. Then a limited number of the fibers may be cut transversely. The bowel wall must not be penetrated. The wound should resemble a pyramid with the base being the surface wound and the apex at the internal opening. The high lying internal opening should not be touched. It will close com-

pletely as soon as the deep portion of the wound has filled in.

After Treatment. Meticulous after care is a "must" in order to have a good end result. Attention must be paid to the incision through the levator ani muscle. Should the incision close before the cavity above the levator has been obliterated a sinus will result and the surface wound will not heal. A gauze pack placed in the cavity at operation is removed in three or four days. After this is removed the cavity is not to be packed again. If the cavity wall tends to fall together a small sheet of rubber can be inserted, so the walls will not adhere. Irrigation with a mild solution of potassium permanganate, about 1:8000 may be useful in cleaning the deep wound also. Excess granulation tissue may be curetted.

Pelvirectal and Retrorectal Fistulas. This type of fistula is rarely seen but may be confused with the aforementioned pararectal type. The abscess is located in the lateral or posterior rectal space and is external to the fascia propria of the rectum. There is seldom an internal opening connected with this type of fistula. The external opening of the pelvirectal fistula is usually at least an inch and a half from the anal verge and slightly posterior to the transverse anal line. The external anal opening of the retrorectal fistula is usually located near the tip of the coccyx and about one inch from it on either side.

Surgical treatment of these fistulas is similar to that of the pararectal type. In extending the incision through the ischiorectal fossa one must be careful not to cut the inferior hemorrhoidal nerves. If these are severed, the nerve supply to two-thirds of the external sphincter muscle is cut off and some incontinence will result.

Summary

A classification of anorectal fistulas resulting from inflammatory processes has been presented. This classification is based on the location of the main track of the abscess in regard to the musculature of the anorectal region.

Some general principles of surgical treatment have been reviewed with emphasis on the idea that fistula internal to the bowel musculature should be opened internally, and fistula external to the bowel musculature should be opened externally, and never through the wall of the bowel above the levator ani attachments.

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Discussion (Abstract)

Dr. Vincent T. Young, Knoxville, Tenn. Dr. Coughlin has presented a most enlightening paper on this fascinating subject. His original classification and general principles of treatment may well mark another milestone in the progress of anorectal fistula.

My reaction to this paper is a hearty agreement in principle to most of its concepts. However, I must confess to certain minor points of disagreement. For instance, a statement is made that "most anorectal fistulae have an internal opening." I take the definition of anorectal fistula to be,—an abnormal communication between the anorectum and skin surface, adjoining viscus or tissue. Therefore, by very definition, I conclude that all anorectal fistulas, without exception, have an internal opening. It is also stated, in reference to retrorectal fistula, that "there is never an internal opening associated with this type of fistula." It is possible that the essayist includes in his classification of anorectal fistula what I might choose to call a sinus. I am interested in hearing the author define anorectal fistula.

It is my understanding that, in the author's experience, the internal opening of the anorectal fistula is usually found at the white line of Hilton which, I believe, is located at the junction of the lower and middle thirds of the anal canal. This does not coincide with my experience. In the vast majority of instances, I find the site of the internal opening at the base of a crypt located at the anorectal junction. I would like to have the author further enlighten us on this point.

A distinctive type of fistula which I think should be included in every classification is that which occurs in the infant. While not common it is not rare, by any means. In the past three years we have encountered 11 cases of this type. They are first seen as an abscess in the anterior perianal region, usually in the first week of life. A fistula results after the abscess is opened or ruptures spontaneously with the internal opening located at the base of a crypt directly opposite the external or secondary opening. The superficial phase of the external sphincter muscle is usually penetrated. There is a definite familial tendency in this type of anorectal fistula. In our 11 cases two pairs of brothers and one pair of sisters were seen. The two sisters were the only females in the group. An interesting sidelight was that the maternal uncle of one of the brother pairs had a fistulectomy performed on him 22 years ago at the age of six weeks.

It has been our policy for many years to correct

surgically all other co-existing pathologic anorectal conditions at the time of the fistula operation, even in the presence of pus. For instance, if in addition to the fistula, the patient was found to have hemorrhoids, fissure, cryptitis, hyperthropic papillae, etc., any combination of these conditions would be dealt with at the time of the fistula surgery. We have found that the patient recovers from the combined procedure quite as quickly and as comfortably and no untoward complications have yet been evident. I am interested in Dr. Coughlin's feeling in this matter.

Dr. Glenn Perry, High Point, N. C. Dr. Coughlin has a most excellent paper. The one thing I would caution about is nomenclature. When you speak of an external opening, what do you mean? Whether it is a primary opening in the anorectal line or a secondary opening, which is your external opening. I believe we are getting a little bit careless about calling it the internal and external opening, and I feel we should make an effort to change that and call it our primary and our secondary openings.

I would like to ask Dr. Coughlin what is his opinion in regard to the anal ducts as a point of origin of fistula in ano. I would like to ask him a second question, one I asked Dr. Williams last year, when he incises a fistula and does not find a primary opening, as all of us have done, what does he do.

Dr. Coughlin (closing). I thought there might be a bit more discussion on this paper, although I am happy to see Dr. Young did not agree with me entirely. A paper should stimulate discussion, to make us think and possibly bring out ideas which have not been brought out by the essayist.

Dr. Young wishes me to define the anorectal fistula. First, Dr. Perry mentioned the terminology in our anorectal fistula, or fistula-in-ano, or sinuses, abscesses, and we loosely combine all of these under the term anorectal fistula. I think more or less in classifications. The fistula should be considered only the complete fistula, and Dr. Young's definition was correct as far as the complete fistula is concerned. However, in defining an anorectal fistula, it is a tract that extends completely or incompletely, bringing in the sinus idea, from the skin to the canal or the rectum, and vice versa,—that to me is an anorectal fistula. The incomplete fistula is certainly a sinus. Because incomplete fistulas are potential complete fistulas, we include them as such, certainly in those resulting from inflammatory processes. Concerning the white line of Hilton, or the intermuscular septum, I believe Dr. Young located it between the middle and lower third; I believe it to be more in the middle and upper third of the anal canal being the narrowest portion of the anal canal. Of course, it marks the line where the fibro-elastic portions of the longitudinal musculature of the rectum traverses the musculature and separates the subcutaneous external sphincter from the internal sphincter. Between this line and the anal rectal line, or the dentate line (again terminology plays a part), is that important upper zone that I think is the middle and upper third of the anal canal or the pecten.

In the subepithelial tissue of the pecten are the glands, lymphatics and capillary network which play a great and important part in anorectal suppurative processes.

In answer to Dr. Perry, as to the etiology of anorectal fistula and the part that anal ducts play in it,—I really do not feel too qualified to talk about etiology. It has always rather defeated me, but certainly we have to take into consideration that here are glands which are lymphatic, and consequently, will react to suppurative processes.

In regard to Dr. Young's statement saying that most of the fistulas he has seen had an internal opening in the crypt, one might say that the crypt is merely a recessed portion of the lower part of the rectum behind the rectal valves between the columns of Morgagni, and they extend in a sac into the pecten. So possibly drawing a line to the internal opening there in the base of the crypt or in the pecten might be rather fine. I do not agree with the idea of crypts being the source, or the sole source of anorectal fistula.

Concerning Dr. Young's custom of doing all needed work at the time of operation, one must consider whether one is dealing with an acute stage, the incision and grading of the abscess, or whether one is doing a fistulectomy. With some of the simpler anterior abscesses and subcutaneous fistulas, even in the presence of acute inflammation, if not too extensive, I would correct all the intrarectal disease. I do not agree on doing all the needed anorectal corrections in the presence of inflammatory tissue and definite suppuration. With an abscess, I like to let the abscess contract and become a definite fistulous tract.

Concerning the internal opening of the fistula-in-ano, in old or in popular terminology, means one found at the white line of Hilton, the high level. Maybe we should speak of the high level opening, or of primary and secondary openings, any one of them being proper. However, an external opening to my mind is one that opens not directly in the skin, nor in the anal derma, or in any portion of it. As far as finding the internal opening is concerned, I think that most of our proctologic statisticians concede that 20 or 25 per cent of anorectal fistula have no internal opening. That is my impression.

Dr. Perry, when I do not find an internal opening, after sufficient and careful examination, I treat it as an incomplete fistula. However, in the subsphincteric fistula where oftentimes one finds the tract going right up to the anorectal musculature below the subcutaneous region, I consider it a complete subsphincteric fistula and open it up as I would had there been an opening in the posterior region. When I say the pelvirectal or retrorectal fistula seldom have a high internal opening, I mean in the rectum, where the main tract actually penetrates the bowel wall. Those are usually due to some extra-enteric fossa, for instance. Retrorectal and retroperitoneal suppurative processes often descend into the retrorectal and pelvirectal spaces; or some prostatic disease in the male, and some adnexal diseases in the female will localize in the pelvirectal spaces.

Granulomas*

A. J. GILL, M.D.,† *Dallas, Tex.*

FOR A NUMBER of years, as a teacher of general and special pathology for medical students and physicians, I have often been impressed with the confusion and differences in understanding which exist regarding the features of granulomas. In short, there is considerable doubt as to the interpretation of the term and the essential characteristics of the granulomatous diseases. Pathologists are not always in full agreement either, and it is because of this that I wish to take the occasion in this brief address to express certain views as to definition and differentiation of pure granulomas from other chronic inflammatory processes. One should hasten to say in the very beginning, however, that pure granulomas without admixtures of other inflammatory elements are not too frequent. With the passage of time the use of terms is subject to great variation and common usage is apt to be quite different from classical definition. This seems to me to be the situation in granulomas.

I believe that most pathologists in recent years have used the term "granuloma" to apply to a rather special type of inflammatory response to injury and have quite generally reserved it for these specific lesions. In an earlier era in pathology the designation "granuloma" was often used to describe a mass made up of granulation tissue. There are many who now use "granuloma" in a broad descriptive way to apply to almost any chronic inflammation, especially if associated with granulation tissue formation. The traditional designation of the total consequence of chronic inflammation as granulomatous would perhaps fit in well with older concepts, since there is nearly always some proliferation of granulation tissue in the repair phases of most chronic injuries. I do not think, however, that we should now accept "granulomatous" as synonymous with chronic inflammation but should circumscribe the definition somewhat more sharply.

To this end I should like to note the extensive discussion of granulomas by W. D. Forbus,[1] who speaks of the *genuine* chronic granulomatous inflammation as a "primary process initiated by a special group of harmful agents which, through their stimulating or injurious effect, bring into primary defensive activity a specialized cellular mechanism" and states that "the mechanism in question is the reticuloendothelial system."

In this point of view, with which I am in substantial agreement, the granulomatous process is a special form of defensive inflammatory mechanism different from the usual acute or chronic inflammations even when these include formation of granulation tissue in the repair phases. It is a response in which elements of the reticuloendothelial system play the most important part. By way of definition then, I believe that "granuloma" should be a designation restricted to mean a purposeful defensive inflammatory response in which the elements of the reticuloendothelial system play a dominant role even though other kinds of inflammatory cells may, and as a matter of fact usually do, participate.

When we speak of the reticuloendothelial system it is probable that all of us do not include the same elements. Here, again, it is frequently astonishing to me to find how much opinions vary, among students and physicians including pathologists, as to the extent of this complex system. In my opinion, vascular endothelium, a large group of tissue cells of undifferentiated types (essentially primitive mesenchymal cells found throughout the reticular and other connective tissues of the body), the reticuloendothelial cells of lymphoid tissues, spleen, liver, and marrow, and also all the great mass of macrophages of both fixed and motile type, whether found in tissues or blood stream, should be included as part of the reticuloendothelial system. This is admittedly a large overlapping, widely distributed group of cells of varying degrees of differentiation and potential. It should be admitted further that

*Chairman's Address, Section on Pathology, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

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mature lymphocytes, plasma cells, and probably many of the other cells of the blood, are ultimately derived from the reticuloendothelial system. However, they differ from the previously listed types mostly by being differentiated and specialized rather than primitive elements which, we believe, have the capacity to respond to proper stimulus and undergo various kinds of special differentiations in the evolution of the true granulomatous process. It is felt by some that, given the needful stimulus to differentiate, reticulum cells may undergo changes in which some become motile macrophages while others remain fixed and participate in the granulomatous inflammation as nonmotile cells. In this concept, then, the reticuloendothelial system most probably has fairly well developed macrophages which may be found almost anywhere in tissue spaces and perhaps in the blood, too. In addition, there appears to be a large reservoir of undifferentiated cells in nearly all tissues which may rapidly become modified and behave as inflammatory cells of either fixed or motile variety. Essentially this view is that those elements which make up the chief inflammatory response in granulomatous disease are a variety of rather primitive cells which differentiate under the specific stimulus of injury. The idea that an inflammatory cell may develop on the spot in tissues which are injured is not objectionable.

It seems to me that part of the misunderstanding which exists in regard to granulomatous inflammation is caused by the varying appearance of the lesions at different times in their evolution, and the changes which may take place in the appearance of reticuloendothelial cells as they are modified by the specific etiologic agents which stimulate the transformation of the reticuloendothelial elements into inflammatory components in the first place. The fact that the morphologic character of granulomatous inflammation may be materially modified by the quantitative and qualitative character of the injurious agent no doubt further contributes to the confusion, as does failure to appreciate the wide distribution of the reticuloendothelial system and the great difference in degree and type of differentiation of these cells when stimulated to react as inflammatory cells.

In *summary*, let me say that it would be desirable to limit the term "granuloma" in a more definite manner with avoidance of the tendency to classify most or all chronic inflammations as granulomatous. We feel that the essential feature of granulomas is the dominant participation of the cells of the reticuloendothelial system and, more especially, the fixed cells differentiated from primitive elements found in all tissues. We feel that lymphocytes and plasma cells, and perhaps other blood cells, probably also are ultimately derived from the reticuloendothelial system, but we prefer to think that these are mature, rather highly specialized cells whose powers of further modification are limited, and that they lack the versatility and adaptability of the more primitive cells which are so conspicuous in the granulomatous defensive response at sites of action of a large group of injurious agents.

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Resurgam:—
To Charles Caswall, M.R.C.S.*

LYLE M. SELLERS, M.D., *Dallas, Tex.*

In 1941, while browsing in the Old Hickory Bookshop in New York I came upon a small book on otology. It was "The Physiology of the Organ of Hearing," written by Charles Caswall on December 15, 1832 and printed for Henry Wix in London in 1833. The cost of the book was inconsiderable, so I purchased it after a most casual inspection and placed it on my bookshelves for some future occasion.

In 1952, while preparing an exhibit on the Development of Otolaryngology for the 1952 meeting of the American Academy of Ophthalmology and Otolaryngology, this volume came up for more careful attention. As I read through it I became intrigued with its classic literary style as well as with its contents, most of which was above its contemporary level and some of which seemed far in advance of its time. It spoke of a man who was great in his thinking capacity and who was most remarkable for his humble attitude and his desire to serve only God and his fellow man.

I made a vain search through otologic and general medical history for information concerning him. Garrison,[1] Garrison and Morton,[2] Stevenson and Guthrie,[3] Politzer[4] and the Bibliotheca Osleriana[5] make no mention of him. Finally I found this item in Sir William R. Wilde's[6] short historical account of otology in the first chapter of his work on Aural Surgery.

"Within the last twenty years there have appeared three small works on the anatomy and physiology of the organ of hearing, by Mr. Swan, Mr. David Tod, and Mr. Caswall. The first of these, from the originality of its ideas, and the speculative theory of its author justly attracted attention in an anatomico-physiological point of view, yet neither it nor the other two with which it is associated should have been enumerated in the history of aural surgery, but that to each were affixed some observations upon the pathology of the ear generally, and its congenital defects in particular. These observations are, however, crude, speculative, and unpractical."

This constitutes then, the only reference to him in medical history that careful search has revealed. But I never lost interest in this man and the book which he wrote. Recently I determined to make a more detailed study of the entire subject.

Noticing from the title page of the book that he had been house surgeon to St. Bartholomew's Hospital in London and that he was a member of the Royal College of Surgeons, I made inquiry of these institutions and received the following two replies:

"It is unfortunate that most of our records were destroyed during the recent war so that we have no internal evidence of Charles Caswall having been here. However I have found his name in an old *Directory* and send these details. CASWALL, Charles, 29 Park Street, Islington—Consulting Surgeon and Accoucher; *Qualifications* M.R.C.S.E. Feb. 9, 1827; one of the Surgeons to the Holloway and North Islington Dispensary; formerly House Surgeon to St. Bartholomew's Hospital, and Senior Surgeon to the Royal General Dispensary, Aldersgate-street; Author of The Anatomy, Physiology and Pathology of the Organ of Hearing and Treatment of its Diseases (sic); Contributor of various papers to the "Medical Gazette".

Despite a careful search I can find nothing further.

Yours sincerely,

(signed) John L. Thornton, Librarian
Medical College Library
St. Bartholomew's Hospital.

"I should like very much to help you in answer to your letter of March 14 * * * but I regret that the records of this College do not contain information about Charles Caswall, except the date at which he became a member of the College. I have, however, found a certain amount of information about him from the early MEDICAL DIRECTORIES and other sources. I enclose a note of all that I have found.

Yours very truly,

(signed) W. R. LeFanu, Librarian.
Royal College of Surgeons of England"

Enclosed Note

"CHARLES CASWALL (or CASWELL)

Born about 1803 or 1804, educated at St. Bartholomew's Hospital, London, and qualified M.R.C.S. on 9 February 1827. Practised in London at 18 Woburn Place, Russell Square, and later at 29 Park Street, Islington till 1853. Served during this period as surgeon to the Royal General Dispensary, Aldersgate

*Chairman's Address, Section on Ophthalmology and Otolaryngology, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

Street, and senior surgeon to the Holloway and North Islington Dispensary.

Moved in 1854 to Waterloo Cottage, Tonbridge, Kent, where he practised till his death of 27 March 1863, aged 59.

Publications:

The Physiology of the Organ of Hearing 1833.

On the Treatment of Gonorrhoeal and Syphilitic Infections with Iodine, *London Medical Gazette* 1834, 15:192.

Large Tumor of the Labium Pudendi Removed. *London Medical Gazette* 1835, 16:77.

Treatment of Hydrocele by Iodine. *London Medical Gazette* 1837, 19:855."

I then made a visit to the Library of Congress in Washington. No reference to the man was available there except a list of the locations of the other known copies of the book in question. There is listed one copy in each of the following libraries: The British Museum, The Library of Congress, the Armed Forces Library, the New York Academy of Medicine, the College of Physicians at Philadelphia, the Pennsylvania Hospital Medical Library and the Philadelphia General Hospital Medical Laboratories. A diligent search of the obituary columns of the contemporary files of the London Times there also failed to find mention of him.

I then turned to Dr. Raymond Courtin, Chief of Anesthesiology at Baylor University Hospital at Dallas, who is of English birth and education. He wrote to his sister Miss Denyse Courtin in London enlisting her aid in the search. Here is her reply:

"Now I have to tell you that so far I have drawn a complete blank. Firstly, Somerset House was no use at all; their records only go back to 1837. I next went to the Records office; no good there, either. Today I have been to the Reference Library, behind the Guildhall, where all kinds of weird and wonderful things are to be found. As you rightly say, as we know his date of death, I thought perhaps the "Times" obituary for the said date might shed some light; not a mention. I then waded through documents referring to the Royal General Dispensary and the Holloway Dispensary. No mention of the man. Everyone I have contacted has been, or tried to be most helpful, and from what they say, this Dr. Caswall just is not sufficiently important a person to have been mentioned in these records I have looked through. I confess now I just don't know where else to go, or who else to contact."

I next wrote to the Town Clerk of Tonbridge, Kent, S. J. Thorne, Esq., seeking Dr. Caswall's birth date and information concerning his parentage or any known descendants. He replied that the town records make no mention of him, but that in the records of St. Stephen's Church, according to the Rev. W. F. G. Hobson, the Vicar, the following is the entry in the Burial Register of the Churchyard:

No. 458. Charles Caswall buried April 1st, 1863, aged 58. Officiating Minister (the Vicar of the time) the Rev. R. L. Alnutt.

That is all except the inscription on the headstone over his grave.

Two letters of inquiry addressed to the Wellcome Museum of the History of Medicine and one to the Registrar of the University of Edinburgh, have remained unanswered, so I must presume that they too, have no information other than that in my possession.

Thus prior to the time of his admittance to the Royal College I have found no information concerning him and his grave seems to have wrapped him in anonymity following his death.

Now just what manner of man was this who was scorned by his contemporary, Wilde, and who at his death seems to have been "not sufficiently important a person to have been mentioned?"

Since "wherefore by their fruits ye shall know them," let us turn to our only remaining evidence,—his book.

In the preface Dr. Caswall clearly recognized the greater crippling of soul and body brought about by isolation from one's fellow men by deafness than by blindness; he offered no one specific cure for deafness (rare in his day) as he stated that there is no one specific cause; that certain parts of the ear are essential to the perception of articulate sound, although he was not correct in the parts he chose; that certain structures and their abnormalities produce certain defects of hearing and finally —"the degree of assistance that may be rendered in these circumstances * * * whereby some benefit may be rendered to our fellow creatures. This is the goal which I desire to attain."

His discussion of the general anatomy of the human ear contributed but little that was new and seems to repeat some of the errors of his times. These errors include listing a fourth ossicle, the os orbiculare, supposedly lying within the incudo-stapedeal joint; mistaking three fibrous bands for three muscles of the midde ear now known not to exist; considering that the tympanic membrane is

not supplied with red blood except in the fetus and during inflammation because of its grey color; describing a membrane similar to the membrane of the round window closing the oval window on which the footplate of the stapes rests instead of the annular ligament that bridges the gap between the edges of the window and the perimeter of the footplate; failing to describe the antrum lying between the middle ear and the mastoid and describing the opening of the posterior end of the posterior semicircular canal into the vertical canal rather than the junction of the two into a common crus. He followed Scarpa's errors in describing the membranous labyrinth,[7] calling the utricle the alveus communis and describing both the canals and the scala vestibuli as opening from it. He described the saccule as a spherical sac—"it is completely closed (and) has no communication with any other part" (p. 21).

On the credit side he described the internal ear as "that part in which the auditory nerve is expanded—the seat of hearing." These nerve endings he placed correctly in the membranous labyrinth (p. 87). He correctly described the chorda tympani as merely traversing the middle ear from its origin in the seventh nerve to its union with the lingual branch of the fifth nerve. He described the membranous labyrinth as filled with fluid and floating in a fluid (p. 21) and he described the scala tympani as abutting the membrane of the round window (p. 21) which he described as a portal of entry for sound into the cochlea! (p. 91). The structure and the function of the eustachian tube he understood perfectly (pp. 10 and 54).

His description of the comparative anatomy is concise and accurate as are the conclusions which he draws from it concerning the physiology of the organ of hearing.

In the realm of the physiology of hearing his conclusions are in advance of his contemporaries even though some of his anatomical premises are in error. It must be recalled here that Flourens[8] in France had published his work identifying the semicircular canals as the end organs of balance four years earlier. Perhaps Caswall should have been aware of this. But the fact remains that to him the internal ear was solely the organ of hearing. "Now, in putting the following question—What is the *use* of the ear? This common and plain reply may be made, to receive sounds, and propagate them to the sensorium. Then another question becomes necessary, viz. What is sound, and by what means is it conveyed from the place of its origin to the organ for its reception? 1st "Sound is a perception of the soul, communicated by means of the ear. * * * Sound however, is distinguished into various kinds, independent of each other; such as force, tone, resonance, simple modulation of voice, and articulation. Now 2ndly By what means are all, or any one, of these distinctions of sound conveyed? * * * The use of the organ of hearing, then, in the human being, is to receive any one of the various sounds above alluded to, which must be conveyed to it by a material substance; and that commonly is air. After receiving the impression of the sound transmitted, the ear conducts it to the sensorium, where its import is, as it were, deposited and understood" (pp. 48 and 49).

Here in a few brief words is the entire basis of the modern concept of hearing as a process of perception (on which are based the above-threshold tests) according to the law of Weber. Sound perception becomes the aim and the end of hearing and so becomes a function of the central nervous system of which the ear is an integral part.

Basing his conclusions on clear deduction he states unequivocally what I am sure will prove to be the correct answer to a question bemusing otologists today—Does sound enter the labyrinth via the oval or the sound window? His answer is, via both (pp. 89, 90, and 91).

By correlating the comparative anatomy of the larynx and of the ear he showed that the structure of the ear varies with the structure of the larynx in an approximate manner in each species so that each species is best fitted to hear the sounds produced by the members of that species. But the human larynx and organs of articulation are heard well by practically all other species thus aiding man in his dominion over lower forms. His approach here while scientific is modulated by a deep religious attitude. This attitude leads him later in the book to reject improperly the law of evolution on purely theological grounds, a field in which he was on less secure ground than he was in the field of otology.

Sir Everard Home had become enamored with the idea that the cochlea could not be considered the essential organ of hearing and transferred the powers of the cochlea to the tympanic membrane along with a process which he called modulation. By modulation he inferred a vague concept of synthesis of harmony and disharmony and a tonal filtration process, so to speak, that prepares sound for perception by the sensorium. He stated these views in the Croonian Lecture delivered by him in 1779 before the Royal Society[9] and in his lectures on Comparative Anatomy.[10] Caswall had this to say about that fantastic idea:

"It is evident from the foregoing quotation, that something more than the modulation of the power or force of sound is alluded to; and that the capacity, or office, with which I conceive the membrana tympani has nothing at all to do, is in the modulation of sounds; nor do I believe the cochlea to have any part in such a capacity; neither, in fact, has any other portion of the organ such a province allotted to it. Sounds are not modulated in any part of the organ." (p. 71)

He stated, however, that the ossicular chain modulates the intensity or force of sound (p. 55) but he recognized that it is not essential for the conduction of sound from the tympanic membrane to the vestibule.

His greatest error seems to have been to assign to the tympanum (middle ear) a power that we now know resides in the organ of Corti—the conversion of mechanical sound waves to nerve (electrical) impulses for propagation to the sensorium. He recognized that such a conversion process must exist and he seized upon the only system known to him likely to fulfill this function. But he stated as his belief that the nerve endings in the membranous labyrinth have a function that is just now beginning to be understood; namely, that those organs now known to be chiefly concerned with balance also perceive sound[11] (p. 88). His error here was in giving to the canals greater ability to discriminate sound than to the maculae.

It is in the recognition of degrees or forms of deafness and his clinical observations of them that his mind leaped ahead of his time as in the following:

"A degree of deafness is perceived, when a common conversation is carried out at one side of a moderate-sized room, and a person afflicted, being at another side of it, cannot hear the discourse until he approaches the party, and then hears perfectly well. Again when it is necessary that the voice should be raised above its usual tone in order to make conversation intelligible, another degree of deafness prevails. And lastly, when, by great exertion of the voice, the sounds issuing are but very indistinctly heard, and in an unconnected manner, a degree bordering on complete deafness is experienced." (p. 95)

Here unquestionably is an early (probably the first) recognition of the clinical entity in perceptive deafness that we now call recruitment of hearing with its narrow field between threshold of hearing and threshold of distortion in which, with slight increase in intensity of the spoken voice the deafened hear perfectly well, and the next step in which with marked increase in intensity, the voice is heard imperfectly if it is understood at all.

In the paragraph just preceding the words quoted above he noted the difference between decreased word reception and decreased tone or noise perception. (Also see p. 107.)

But again because he did not know of the organ of Corti he did not place correctly the sites of the lesions producing the various forms of deafness.

Diseases of the external and middle ears are described quite accurately and the influence of enlarged tonsils (p. 98) and nasal polypi (adenoids?) on the patency of the eustachian tube is recognized. He mentioned also malformations of the fenestrae (otosclerosis?) as being causes of partial deafness. (p. 106)

Complete deafness he recognized as being caused by the labyrinth (or nerve) as complete deafness may occur in the presence of a normal tympanum (p. 104).

He pled for a careful examination in order to find the site of the causative lesion (p. 107) for only in recognizing the type of deafness present and its specific cause can there be hope of relief of the affliction. This hope he felt could be attained best by prophylactic and preventive otology and by early treatment in established cases. In this connection he recognized disease in the parent as a cause of

deafness in the child. How recent has been our recognition of maternal roseola occurring during the first trimester of pregnancy as a cause of deafness in the child!

His approach to treatment is a standard for otology today, as witness:

"The affections of the auditory organ for the most part render the sufferer almost a nonentity in social society; and, consequently, induce him to seek relief by whatever means it can be procured. Stimulated by hope, he accepts assistance (or what he conceives to be such),—and sometimes from the hands of those who seek their own enrichment at the expense of the sufferer's credulity,—and, eventually, not one iota of IMPROVEMENT has been acquired. Thus the profession in general becomes denounced, in consequence of the rapacious appetite of pretenders for gain."

He then laid down the precept that the principles of otologic surgery and treatment are those of general surgery and medicine. He thus decried incising (bleeding) or leeching acutely inflamed tissues in and about the ear as being likely to cause spread of infection (erysipelas), and venesection as depleting the patient's reserve for recovery (pp. 113-114).

He advocated plastic surgery for restoration of the auricle for cosmetic purposes (p. 110). He advocated and practiced paracentesis of the tympanic membrane and opening and draining of the mastoid cells for acute suppuration (p. 112). For the relief of tubal obstruction he advocated Cooper's[12] procedure of paracentesis, catheterization of the tube and removal of enlarged tonsils and nasal polypi (adenoids?) (p. 115).

He recognized diseases of the auditory nerve as being secondary to a remote or general disease, and its relief being dependent upon recognition and correction of the causative disease.

His recognition of his lack of knowledge, the reasons for it, the means for its correction and his approach to his work stand today unsurpassed in the annals of medical honesty and humility.

" . . . and although there are many volumes containing dissertations on Deafness, I shall doubtless meet with many persons who will concur with me in asserting that but very few are extant, from which any knowledge can be obtained of the many causes producing this distressing affection. This can readily be accounted for, and more especially so in this country, by observing the difficulty that has hitherto been raised against postmortem examinations and dissections. Up to the present period every obstacle has been offered to the persevering pursuer of morbid anatomical research; and a flat denial has in most instances followed the (apparently inhuman) request for examination. Thus we are not at a loss for a reason why so little knowledge has been attained of the physiology and pathology of the human ear; and when we consider its minute and intricate structure, and the great care and labor necessary for the obtaining information by dissection, (all obstacles to such a source being overcome,) we can easily conjecture how very soon the ardour for inquiry becomes dormant, unless stimulated by an anxiety tantamount to that displayed in searching for the philosopher's stone. What, then, has been wrought by my attempt at inquiry, that I presume to add a volume (although small) to the already inefficient collection? I reply; Very trifling indeed, are my pretensions; but it is step by step that we must proceed, and not expect as yet to be super-human in the acquisition of knowledge: the little already known has led to further inquiries; and the addition I may be enabled to make may still be an inducement for future investigation by those whose intellectual capacity and powers of perseverance will place me, in comparison, as a shadow to the substance. My desire is, to add to the already incomplete productions another, (though perhaps less efficient than any,) containing views not before divulged, hoping something beneficial may be established from them by those who are competent to undertake the subject than myself."

This then is the man whose death was unrecorded by the contemporary press simply because he was just not sufficiently important a person and whose only mention in medical history was condemnatory. The otologic surgeon who penned it should have been more ready to recognize his fine mind and its merits. It was a mind capable of careful observation and astonishingly accurate philosophical deduction.

For nearly four score and seven years in the Churchyard of St. Stephen's Church at Ton-

bridge in Kent his head has "rested upon the lap of Earth ** to Fortune and to Fame unknown." But he has slumbered securely on the bosom of God whom he worshipped and served. His epitaph might well have been a paraphrase of that on the tomb of the Unknown American Soldier—"Here rests in honored glory a British surgeon known but to God."

But with both Spiritual prophecy and Mortal justice the inscription reads simply—

Sacred to the Memory of
Charles Caswall, Surgeon,
Who died March 27th, 1863
Aged 59 years
RESURGAM
(I Will Arise)

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Malignant Tumors of the Spermatic Cord and Testicular Tunics*

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Two cases are added to the rare group of tumors arising from the spermatic cord and testicular tunics.

WHILE TUMORS of the testes are relatively frequent, neoplasms of the spermatic cord and testicular tunics are rare; so rare, as pointed out by Thompson,[16] that their interest is more academic than of clinical importance.

The discovery, in 1950, of a leiomyosarcoma of the spermatic cord, and the finding in 1952 of a rhabdomyosarcoma of the tunica vaginalis in a four year old boy, have prompted us to report these uncommon neoplasms.

In January, 1952, Fitzpatrick, Orr, Glanton and Hayward[4] reviewed the world literature on spermatic cord tumors from the time of Thompson's[16] excellent report in 1936 and added two cases. This exhaustive review brought the total number of cord tumors to 286. The case of a leiomyoma, reported by Zuckner and Aronberg[20] in August, 1951, was not listed in their compilation. In February, 1952, Sherwin and Bergman[15] discussed a leiomyosarcoma of the spermatic cord. In June, 1953, Wessel[19] reported a compilation of malignant tumors of the spermatic cord and his case of a leiomyosarcoma brought the total number of malignant neoplasms to 81.

Other cases of primary spermatic cord tumors recorded in the literature since the report of Fitzpatrick *et al,* but not yet tabu-

*Read before the Section on Urology, Southern Medical Association, Forty-Eighth Annual Meeting, St. Louis, Mo., November 8-11, 1954.

lated, are: A rhabdomyosarcoma by Hansen, Enos, Park and Postel;[6] a fibrosarcomata by Laumonier and DePaulis;[11] a leiomyosarcoma by Herbut;[8] a primary sarcoma by Pobil, Diaz and Diaz;[13] a primary seminoma of the spermatic cord by Pacheco;[12] a fibroma by Jackson and Robinson;[10] a fibrolipoma by Hashemain;[7] and a sarcoma by Thompson.[17]

Our case of leiomyosarcoma and lipoma brings the total number of reported malignant tumors of the spermatic cord to 88 and the total number of benign and malignant neoplasms to 299.

In the late literature, three unusual spermatic cord masses have been reported. These swellings are not considered true tumors of the cord, according to the classification of Hinman,[9] and they are not tabulated in the total compilation. They are: an adrenal cell rest tumor reported in 1949 by Gualtieri and Segal;[5] an organized thrombus reported in 1952 by Salomon and Sachs;[14] an extratesticular, extravaginal benign cyst reported in 1953 by Albers and Bielstein.[2]

Tumors of Spermatic Cord

According to Hinman and Gibson,[9] 90 per cent of extratesticular tumors within the scrotum occur in the spermatic cord. Sixty-four per cent of these tumors are benign, whereas at least 95 per cent of testicular tumors are malignant. Slightly more than 98 per cent of spermatic cord tumors are mesodermal in origin. No predisposing cause is known. These tumors arise from various elements of the cord and from remains of the wolffian body.

Lipoma is the most commonly reported tumor of the spermatic cord. Mixed tumors and fibromas, along with the lipomata, make up the majority of benign neoplasms.

Most authors have accepted Rubaschow's tabulation of three cases of carcinoma of the spermatic cord. According to Hinman and Gibson,[9] only one authentic instance of carcinoma of the spermatic cord exists in which the origin was thought to be the remnants of the wolffian body. Cole and Campagna[3] in 1942, reported a case of carcinoma (seminoma) and Pacheco,[12] in 1953, discussed a case of primary seminoma of the spermatic cord. Wessel[19] states that of the teratomatous tumors reported, it is probable that most of them were sarcomatous.

Sarcoma is the most frequently reported malignant tumor. Next to lipoma, it is the most common tumor of the cord. Sarcomas occur as fibrosarcoma, myxosarcoma, liposarcoma, spindle cell or giant cell sarcoma or in various combinations. Fibrosarcoma is the most common type. Rhabdomyosarcoma and myosarcoma are very rare. Our case of leiomyosarcoma of the spermatic cord is the sixth one to be reported.

Many authors think these growths have their origin in a benign tumor of long duration followed by malignant degeneration. These mesoblastic tumors usually appear to originate at the point of junction of the epididymis with the various elements of the cord and their union by connective tissue. Sarcomas of the cord are usually scrotal and uncommonly inguinal; the growth rarely extends up into the inguinal canal as it did in our case.

In general, spermatic cord tumors are usually easily recognized but occasionally it is impossible to make a definite preoperative clinical diagnosis. Cord tumors do not present any typical characteristic symptoms. Most of the benign growths are circumscribed and movable. A mass palpable above a normal testicle and epididymis certainly suggests an extratesticular tumor. Conditions which are liable to be confused with cord tumors are hernia, hydrocele of the cord, cyst of the cord, tumor of testicular tunics, spermatocele, hematocele and chronic inflammatory lesions. It is to be remembered that soft lipomas and myxomatous tumors may transilluminate. A malignant tumor should be suspected if the mass is fixed to the cord.

Tumors of Testicular Tunics

Tumors of the testicular tunics are even more rare than spermatic cord tumors and, as emphasized by Hinman[9] and Thompson,[16] are difficult to distinguish from those arising in adjacent structures.

Of these neoplasms, tumors of the tunica vaginalis are most prevalent in the reported literature, a majority occurring in younger individuals. In this respect, they are similar to tumors of the testicle. A majority of these tumors are benign, sarcoma being the common malignant tumor of the tunica vaginalis. Waller and Hellwig[18] stated that 51 cases of

sarcoma have been reported in the world literature.

Our case, a primary rhabdomyosarcoma showing striated muscle and arising from the cremasteric fibers, belongs to the rare group of malignant sarcomas of the testicular tunics. To our knowledge, no other case of rhabdomyosarcoma of the testicular tunics has been found, although such tumors of the spermatic cord have been reported.

As pointed out by Herbut,[8] all tumors within the scrotum should be considered testicular in origin and malignant until proved otherwise. Our preoperative diagnosis was that of testicular tumor; this brings out the difficulty of differentiating extratesticular tumors adjacent to the testes from testicular neoplasms.

Treatment and Prognosis

In all cases of tumor of spermatic cord, epididymis or testicular tunic in which there is some question as to the benignity of the growth, exploratory operation is indicated. If in doubt a frozen section must be done. It is an accepted opinion, if the growth is benign, that simple excision is all that is necessary. If the tumor is malignant orchiectomy is performed with high ligation of the cord. When a tumor is definitely earmarked as malignant preoperatively, the cord, tumor and testicle are removed through an inguinal incision, after high ligation at the internal ring.

Following orchiectomy, the patient should receive the same deep x-ray therapy accorded testicular tumors. According to Ackerman and Regato,[1] liposarcomas are radiosensitive, and angiosarcomas have shown surprising radiosensitivity. Other types of sarcoma are more radioresistant. Deep therapy can afford considerable palliative effect and in a few instances has salvaged patients when surgery has failed.

Since sarcoma spreads as frequently by the blood stream as by the lymphatics, radical dissection of the iliac and preaortic nodes does not seem indicated.

The prognosis and the results of treatment of malignant tumors of the spermatic cord and testicular tunics remain to be defined. The prognosis must be guarded. Little is known about the prognosis of malignant tumors of the spermatic cord, mainly because so few end results of treatment have been recorded in the literature. Sarcomas tend to spread locally and often recur. Only when there is skin involvement, is there spread to the inguinal nodes. Metastases may develop after as long as 14 years, as in the case of Fitzpatrick *et al.*[4]

Case Reports

Case 1. J. L., a 62 year old, white bachelor farmer, entered Evangelical Deaconess Hospital on February 18, 1950, with a chief complaint of a mass in the left scrotum and inguinal region.

He had first noticed a small mass in left scrotal sac about six months prior to admission. There was no history of trauma prior to discovery of the scrotal swelling. The mass gradually increased in size and new masses appeared higher up in left scrotum and in left inguinal region. At the time of admission, the slightly tender growing masses had practically incapacitated him. The area had never become red or inflamed, nor had it ulcerated or drained. Occasionally the patient had a dull pain in the lower left quadrant. He had no gastrointestinal nor urinary symptoms. There was no weight loss.

The patient had always enjoyed good health. He denied such illnesses as tuberculosis, diabetes, nephritis, venereal disease and allergies. This was his first hospital admission. Review of systems was entirely negative except for his hearing which had become progressively worse for the past 10 years.

Examination. Patient was a well developed, rather thin, white man, appearing somewhat older than his stated age. Other than impaired auditory acuity the head and neck were essentially negative. Cardiovascular and pulmonary systems were normal. Blood pressure was 120/80. Abdominal examination revealed no abnormal masses. A large irregular, nodular, hard, nontender, lemon-sized mass was palpable in the left upper scrotum. Induration and nodularity extended up into the spermatic cord and inguinal region. Medial to and below the large solid knotty mass was a softer pliable mass. A testicle of normal size was palpable below the masses and in the lower portion of the scrotum. The skin overlying the masses was slightly erythematous but movable. None of the masses transilluminated. The left inguinal nodes were enlarged and indurated. The right testicle and scrotal contents were normal.

On rectal examination, the prostate presented a grade 2 hypertrophy, was smooth, not fixed or tender and elastic in consistency.

Special Studies. The urine, blood count and blood NPN were normal. Serologic test for syphilis was negative. Excretory urographs showed the kidneys normal in size, shape and position. The function was normal on both sides. There was no evidence of obstruction of either ureter. Pyelo-ureterographs were normal. The excretory cystogram showed a filling defect in the base of the bladder which was thought to be due to enlarged prostate. Radiogram of chest showed heart and diaphragm normal. The lung fields

were clear and free of disease. There was no evidence of active process in either lung.

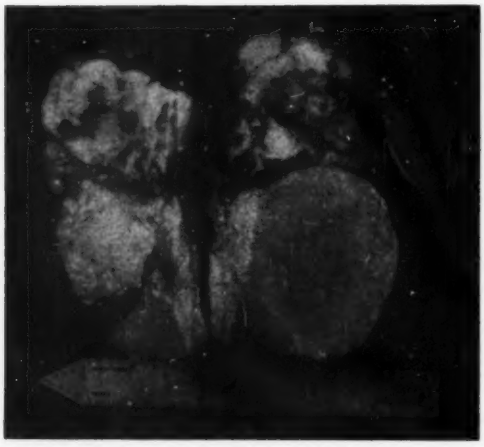
A *preoperative diagnosis* of sarcoma of the left spermatic cord was made.

Operation. On February 21, 1950, a left orchiectomy was performed under Sodium Pentothal, nitrous oxide ether anesthesia. A left inguinal incision was carried down into the upper scrotum. The external oblique aponeurosis was opened through the external ring. The thickened nodular spermatic cord was isolated at the internal ring. The cord was ligated in sections. The peritoneum was opened and no retroperitoneal nodular masses were felt. The large nodular spermatic cord and mass were markedly adherent to the scrotal fascia. The testicle, which felt normal, the mass and the spermatic cord were dissected free and removed. Palpable inguinal nodes were excised. The inguinal canal was repaired.

Pathologic Findings. The specimen consisted of an irregular shaped mass of tissue, measuring 150 by 140 by 170 mm. At one side of the specimen was a normal appearing testis and epididymis within the scrotal sac. Adjacent to this was a large soft yellow mass of tissue, measuring 90 mm. in diameter, consisting primarily of fat. In the region of the spermatic cord was a very firm white mass of tissue, measuring approximately 80 by 50 by 50 mm. This was nodular in character and for the most part was white, but showed yellowish areas of necrosis. At the upper portion of the cord this tumor had been cut across and apparently some had been left behind. The tumor tissue was firm and fibrous in nature (Fig. 1).

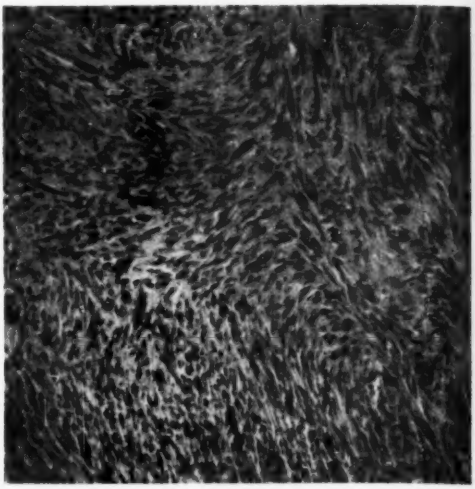
Microscopic section through the large fatty mass showed simply fat. This was a simple lipoma. Section through the firmer areas of tumor tissue showed elongated spindle like cells with hyalinization in the firmest areas. In other areas the tumor was very cellular and these spindle shaped cells were very irregular in size and shape. There were a moderate number of mitotic figures. The cells showed some palisading and some arrangement in whorls. No cross-striations were seen. There were some areas of necrosis and abscess formation within the tumor. In some sections there were larger cells which seemed to be giant cells, representing the nuclei of several degenerated cells (Figs. 2 and 3).

FIG. 1



Gross specimen shows normal testicle and epididymis. Below this is a large soft lipoma. In the region of the spermatic cord is a firm white mass, the leiomyosarcoma.

FIG. 2



Section through leiomyosarcomatous tissue shows elongated spindle-like cells with hyalinization in the more firm areas. In other areas the tumor is very cellular and spindle shaped cells are very irregular in size and shape. Cells show some palisading and arrangement in whorls.

FIG. 3

High power of figure 2. Note a moderate number of mitotic figures. No cross-striations are seen.

FIG. 4

Lateral view of recurrence in upper scrotum and lower inguinal region.

Diagnosis. Leiomyosarcoma of the spermatic cord and lipoma of the spermatic cord.

Course. The postoperative course was uneventful. Deep x-ray therapy was begun on the thirteenth postoperative day. He was discharged on the sixteenth postoperative day and daily treatments with deep x-ray were continued on an out-patient basis until he had received 6,120 roentgen units.

He was readmitted to the Deaconess Hospital one year later, on February 25, 1951, complaining of a recurrence of tumor in the left upper scrotum and groin. The painless tumor had grown slowly during the past year. He had felt well and had worked daily on his farm. There was no known weight loss.

Examination. The abdomen was soft; liver and spleen were not enlarged. There were no palpable abdominal masses. In the upper left scrotum and groin was a hard, egg-size, somewhat movable mass. The overlying skin was adherent and red. One node was palpable in the left femoral triangle (Fig. 4).

Special Studies. Radiograph of the chest showed the heart to be normal; the lungs were clear without evidence of metastases. Complete blood count showed RBC of 4,840,000, hemoglobin, 13.5 Gm. and WBC of 6,000.

The *preoperative diagnosis* was a recurrent leiomyosarcoma of the left spermatic cord.

Operation. On March 2, 1951, under Sodium Pentothal, nitrous oxide and ether anesthesia, an elliptical incision was made around the egg-sized tumor in the upper scrotum. The tumor was excised, removing the overlying attached skin with it. By sharp dissection, indurated areas, scar tissue, inguinal and femoral nodes were removed in a block. The femoral vein and artery were dissected free. Since indurated tissue surrounded the saphenous vein, it was ligated. Skin closure was done by using a modified Z plastic.

Pathologic Findings. The specimen consisted of a tumor, measuring approximately 50 mm. in diameter, covered on three sides by skin. The central part of the tumor showed soft yellow areas of necrosis and some reddish areas of hemorrhage. In one area there was attachment to the skin.

Section of specimen showed squamous epithelium beneath which was an infiltrating type of tumor tissue, composed of spindle shaped cells with some palisading and a number of giant nuclei and an occasional mitotic figure. There were large areas of necrosis. There was no attempt at encapsulation.

Diagnosis. Recurrent leiomyosarcoma of the spermatic cord.

Clinical Course. Postoperatively, the inguinal-femoral portion of the wound sloughed, and at the time of discharge on April 1, 1951, the wound was granulating well.

The patient has not been seen since June 16, 1951. His family doctor wrote on August 7, 1954, that the patient said he was too busy on the farm to make a visit to St. Louis. According to his doctor, the patient feels well, has a good appetite, has no pain and has gained weight. There are no palpable abdominal masses, organs or lymph nodes.

Case 2. J. F., age 4 years 6 months, was admitted to the Deaconess Hospital on October 28, 1952. The mother first noticed an enlargement of the left testicle in March, 1952, seven months earlier. At that time a pediatrician told the mother that the enlargement transilluminated and that it was most likely a hydrocele. She was advised to watch it and report any increase in size. The mother became alarmed in October, 1952, when the mass felt hard and she consulted another pediatrician who advised operation. There was no history of trauma.

Other than "three-day measles" the past history was negative.

Examination. The patient was a well developed and nourished boy. The general physical examination was negative. The abdomen was soft without tenderness; there were no palpable masses.

The left testicle was enlarged, 6 cm. in its long axis, smooth, firm and nontender. The mass did not transilluminate. It was thought that the head of the epididymis could be differentiated.

FIG. 5

Gross specimen of rhabdomyosarcoma. Surface of tumor mass is smooth; spermatic cord is attached superiorly. Note the normally developed testis and epididymis in the upper part of tumor mass. Attached to the lower pole of the testis is a firm yellowish mass.

Special Studies. The urine, complete blood count and blood NPN were normal. Friedman and cardiolipin tests were negative.

Radiograph of the chest showed the heart and diaphragm normal. There were moderately increased markings in the lower part of both lung fields extending from the hilar regions. These were probably due to recent respiratory infections or some old bronchial disease. There was no evidence of metastases. Excretory urographs showed normal functioning kidneys without pathology. The *clinical impression* was testicular neoplasm.

Operation. On October 31, 1952, under drop ether anesthesia, a left orchiectomy was performed through a left inguinal incision. The spermatic cord was sectioned and ligated at the internal ring, the cord and scrotal tumor were dissected free and removed.

FIG. 6

Microscopic section shows a cellular tumor. Cells show some elongated fibers with intracellular substance which resemble muscle tissue.

FIG. 7

High power view of figure 6 which shows cross-striations.

Pathologic Findings. The specimen consisted of a rounded oval mass of tissue, measuring 40 by 30 by 25 mm. The surface of the tumor mass was smooth. One end was attached to the spermatic cord. The upper end of the tumor mass measured approximately 35 mm. in diameter and consisted of a sac-like structure in which was a normally developed testis and epididymis. The visceral layer of the tunica vaginalis was smooth and glistening and the testis was bluish in color, and measured 15 by 8 mm. Attached to the lower pole of the testis was a firm yellowish mass of tissue, approximately 25 mm. in diameter. The parietal portion of the tunica vaginalis was thickened throughout the entire portion and this extended up and surrounded the epididymis. There were nodules within the mass of white firm tissue. The tumor tissue was firm and the cut surface was glistening and yellowish-white in color (Fig. 5).

Microscopic section showed a cellular tumor the cells of which showed some elongated fibers with an intracellular substance which resembled muscle tissue. Cross-striations were visible with hematoxylin and eosin, but were more pronounced with iron and hematoxylin stain. No giant cells were seen. The tumor came up and involved the visceral portion of the tunica vaginalis at the lower pole, but did not invade the testis proper or the tunica albuginea. The tumor surrounded the epididymis. This was a well differentiated rhabdomyosarcoma arising apparently from fibers of the cremasteric muscle in the wall of the scrotal sac (Figs. 6, 7 and 8).

Diagnosis. Rhabdomyosarcoma of the cremasteric muscle layer of the testicular tunics.

Clinical Course. The patient had a completely uneventful postoperative course. The wound healed per primum and he was discharged eight days after surgery. Due to the patient's age and the well-differentiated nature of the tumor, it was agreed upon by the pathologists and roentgenologists not to irradiate.

Examination two years later, in September, 1954,

FIG. 8

Cross-striations more pronounced with iron and hematoxylin stain.

revealed the patient to be a well growing boy. There was no evidence of metastases. X-ray examination of the chest was negative.

Summary

Malignant tumors of the spermatic cord and testicular tunics are rare.

A case of leiomyosarcoma and lipoma of the spermatic cord and one of a rhabdomyosarcoma of the cremasteric layer of the testicular tunic are presented.

The leiomyosarcoma is the eighty-eighth malignant neoplasm to be reported. This leiomyosarcoma along with the lipoma brings the total number of reported benign and malignant tumors of the spermatic cord to 299.

Thirty-four per cent of spermatic cord tumors are malignant. Sarcoma is the common malignant neoplasm of the spermatic cord and testicular tunics.

No other case of rhabdomyosarcoma of the testicular tunics has been found.

Tumors in or near the testis must be regarded as malignant until proved otherwise. Treatment of malignant tumors of the spermatic cord and testicular tunic is the same as that given testicular tumors.

The efficacy of radiation therapy is not definitely known. Radical dissection of the retroperitoneal nodes does not seem indicated.

The prognosis is guarded. Metastases may occur late. Our patient with a leiomyosarcoma and the one with a rhabdomyosarcoma are living and well without apparent recurrence three and two years respectively after surgery.

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Discussion (Abstract)

Dr. Lloyd E. Deddens, Jackson, Miss. I feel highly honored to have been asked to open the discussion of this first paper presented before this group. May I compliment Dr. Cannon on presenting such an interesting paper on a rare subject. However, I feel very much like Will Rogers in that, except for experience with one case, all I know about this is what I have read in the literature.

In reviewing the files at our two local hospitals, one of which has had an average yearly admission of 12,000 patients during the past 10 years and the other an average of 6,000 patients, I was able to find only two cases of malignant tumors of the spermatic cord. One was that of a 78 year old white man who had noticed a swelling in the left scrotum for several months. We did a high ligation and orchidectomy. The pathologic diagnosis was leiomyosarcoma. The other case was that of a 75 year old colored man who had a mass removed from the right groin by a general surgeon. Eight months later he was readmitted for a recurrence of a nodule in the scar. X-ray film of the chest at this time showed multiple metastatic nodules in the lungs. The original diagnosis was sarcoma, probable leiomyosarcoma of the spermatic cord. No follow-up was available on either man.

As Dr. Cannon has emphasized in his summary, all tumors in or near the testes must be regarded as malignant until proved otherwise. This should become axiomatic when dealing with these scrotal masses. He has emphasized the conditions which must be differentiated, as hernias, hydroceles of the cord, lipomas, and chronic inflammatory conditions. The point to be made is whether one is dealing with a benign or malignant tumor. If in doubt, it is not amiss, to expose the cord in the inguinal region where a tourniquet can be applied, following which the scrotal contents can be exposed, a frozen section made and, if malignant, high ligation of cord and removal of scrotal contents can be done on the affected side. If benign, simple enucleation can be carried out.

I should like to re-emphasize several points Dr. Cannon mentioned in his paper: (1) All tumors in or near the testicle should be regarded as malignant until proved otherwise, and this can best be done by exploratory operation. Since there is no laboratory test which can be used to aid us in making a diagnosis and, since early detection and removal is the best "cure" for malignant new growths, I feel

that the procedure outlined above should be strongly recommended. (2) While the role of deep postoperative irradiation is not definitely known, all are agreed that it should be given over the preaortic lymph node area after these new growths have been removed and also to the operative areas to take care of any spillage. (3) Since metastases may occur late, frequent chest x-ray films should be made in the hope that early detection may be possible and help from the chest surgeon may be anticipated.

Clinical Applications of Zone Electrophoresis of Serum Proteins*

W. G. RICE, M.D., and with the technical assistance of May Yamaoka, M.T., *Augusta, Ga.*

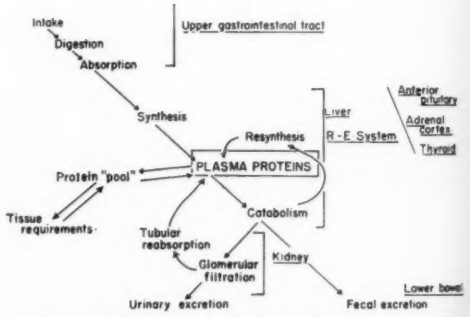
The recent introduction of this method for determining the electrophoretic pattern of serum globulins, rather than with the more cumbersome and expensive original Tiselius method, permits more wide-spread use of such data in clinical medicine.

ZONE ELECTROPHORESIS of serum provides a practical means of studying the serum proteins. Although originally developed as a tool for biochemical research, the method is readily adaptable to the less exacting requirements of clinical medicine. Since the inception of the method, research workers have attempted to secure a degree of quantitative accuracy that is both unnecessary and not significant when applied to clinical medicine. When this point is understood, the procedure becomes more generally useful and less formidable than the complicated calculations and apparatuses described would suggest.

Basis of Protein Physiopathology

The central position of the serum or plasma proteins in the body economy is illustrated diagramatically in figure 1. Despite the many variable factors which play a role in the maintenance of the circulating proteins, these are maintained at an amazingly constant level in health. The diagram also serves to illustrate the major factors which may produce depletion or alteration in the serum protein fractions. The relationship of these processes to particular organs or systems is shown and it is readily apparent that pathologic processes in these many organs may lead to disturbances of the circulating proteins. Marrack and Hoch[14] have summarized the clinical importance of the serum proteins in disease. Homburger and Petermann[9] have classified significant changes which occur as follows: (1) hypoproteinemias, (2) hyperproteinemias, (3) dysproteinemias, and paraproteinemias. The hypoproteinemias represent a lowering of the total circulating serum proteins; hyperproteinemias represent increases in the total protein; dysproteinemias include alterations in the distribution of the proteins which are

FIG. 1



Simplified diagram illustrating the major processes which maintain the plasma proteins at a constant level. The underlined organs have a definite role in the various functions outlined and pathologic processes in the organs will eventually lead to changes in the plasma proteins.

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usually associated with one or more of the other changes; paraproteinemia is the occurrence of abnormal proteins in the serum or plasma and notably occurs in multiple myeloma[2] and Waldenström's macroglobulinemia.

Alterations in the serum proteins may occur as the result of prolonged deficiency in dietary protein. Such is illustrated by kwashiorkor and starvation syndromes.[12, 31] Unless there is an associated irreversible lesion these are rapidly corrected by the administration of adequate protein. This is illustrated by the case in figure 3. Similar deficiencies, however, may develop in the presence of a normal intake, when there is disease of the upper gastrointestinal tract. This may take the form of lesions which interfere with absorption such as occurs in pernicious anemia,[19] scirrhus carcinoma of the stomach,[9] or celiac syndromes or tropical sprue.[1] Deficiency may also be produced by competition for essential proteins by helminthic parasites. Absence of digestive enzymes in fibrocystic disease or chronic atrophy and fibrosis of the pancreas may also produce deficiencies in the area of defective digestion and absorption.[30]

In the lower gastrointestinal tract excessive loss of protein may be the result of prolonged severe diarrhea or exudation and hemorrhage. This is exemplified by the hypoproteinemias that characterize ulcerative colitis.[18]

Synthesis of albumin probably occurs in the liver[16, 21] and that of gamma globulin in the reticuloendothelial system.[17] This is a continuing process, balanced by constant catabolism and controlled by tissue demands and some hormones, of which the anterior pituitary growth hormone, adrenal cortical hormones and thyroid are known to take part.[7] This ebb and flow is carefully balanced in health maintaining a constant level of the various plasma protein constituents balanced against the protein "pool" and the normal requirements of the body tissues. Neoplastic disease by excessive demands on the protein "pool" may produce hypoproteinemias. In the same area, defective synthesis of albumin may occur in chronic hepatic disease or of gamma globulin in disease of the reticuloendothelial system. Primary agammaglobulinemia with atrophy of the lymphoid structures is a condition of selective defective protein synthesis.[8] Much remains to be learned about this and allied deficiencies such as idiopathic hypoproteinemia in which deficiency in circulating gamma globulin is associated with hypoalbuminemia. In this latter condition it has been shown that excessive protein catabolism plays an important role.[25]

In certain cases of hypoproteinemia the endocrine glands have been implicated. Hypoproteinemia in Cushing's, Addison's disease or hypothyroidism exemplify the effect of the endocrine glands on the ebb and flow of protein physiology. Increases in the gamma globulins occur in normal or excessive responses to infection accompanied by reactive proliferation of the cells of the reticuloendothelium.

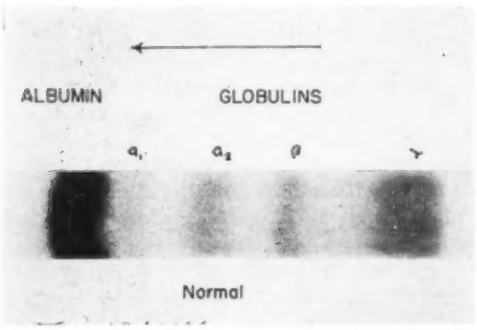
Ordinarily the kidney conserves the protein. Such proteins as normally escape through the glomerular membranes are believed to be "recaptured" by the renal tubular epithelium.[20] However, when loss through the glomerular membrane is excessive as in acute glomerulonephritis, the tubular function may be overwhelmed and the excessive protein be lost in the urine. Similarly, if there is physiologic or physical damage to the renal tubular cells, the phenomenon of reabsorption may become ineffective and a protein depletion develop. The enzyme-rich renal tubules may also play a part in the catabolism of protein.

This then summarizes the general background for the approach to abnormal patterns of the serum proteins. The original "loss and lack" theory has been modified and displaced by the recognition of the important roles of synthesis[15] and catabolism in the maintenance of the serum protein levels. The wide variety of systems and organs involved makes the determination of the pattern in serum proteins of value and importance in the clinical analysis of many varied pathologic processes, particularly those occurring in the endocrine glands, the liver, pancreas, kidney and both upper and lower gastrointestinal tracts.

Zone Electrophoresis

The use of filter paper strips for physical separation of the major components of the serum proteins was first used in modern times by Durrum[5] and Tiselius.[29] Since then it has received wide usage in research procedures having been used for proteins, polypeptides, amino acids, enzymes, lipoproteins and mucopolysaccharides. The theory, uses and variations in technics are summarized and discussed by Tiselius and Flodin.[29]

FIG. 2



Normal protein pattern. (Stained with naphthalene black 12B).

In general the method makes use of the amphoteric quality of proteins and the differences of electrical charge which the various protein molecules carry in solution at a given pH. The proteins are moved by the force of a constant electric current, the amount of movement being proportionate to the force applied which is in term proportional to the electrical charge carried by the protein molecule. The protein molecules are retained in position, after movement, by an inert substance such as starch or cellulose paste, agar or most usually the cellulose mesh of filter paper strips. Thus at a buffered pH of 8.6, the proteins all carry a negative electrical charge and move towards the anode. Albumin carrying the greatest charge moves farthest, and gamma globulin carrying the least charge moves the least distance. The normal protein pattern stained by naphthalene black 12B is shown in figure 2.

Theoretically the distance moved should be exactly proportional to the isoelectric point of the particular protein but such assumptions are precarious. A number of uncontrollable indefinite factors, applied variably to the protein molecules, interfere with their free motion. For instance, the size and shape of the protein molecules may influence the degree of movement. Globular proteins of small size such as albumin move more easily through cellulose than does a linear protein such as fibrinogen. The electrical charge of the supporting cellulose fibres, the occurrence of convection currents and the occurrence of endosmosis (or reverse flow of the buffer) also modify the unrestrained movement of the molecules.

Quantitation. There have been frantic and involved attempts to translate the amounts of serum on the filter paper into reproducible accurate quantitative terms. This reflects an unnecessary attempt to translate the results into terms of electrophoresis by the moving boundary technic of Tiselius. Since microtechnical amounts of serum are applied to the filter paper, accuracy becomes difficult. The possible methods by which quantitative results may be determined are as follows:

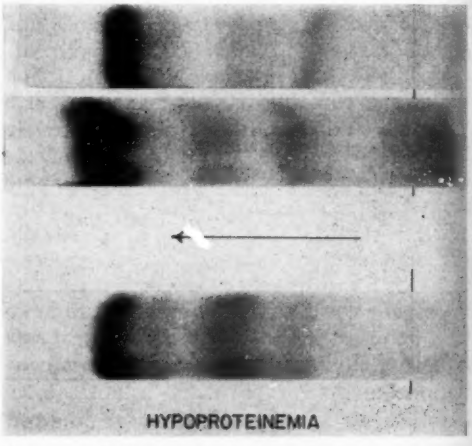
1. Elution of the protein and multiple determination from transverse strips by methods of nitrogen chemistry (Micro-Kjeldhal, etc.).

2. Fixation and staining of the protein *in situ*, with subsequent elution of the dye and determination of the amount of photometric measurements of dye intensity.

3. Measurements of light transmittance through serial transverse slits after staining by means of scanning devices. This method has been modified by using reflected together with transmitted light.

Each method represents an improvement in convenience over the preceding one. The first method, while accurate, is long and involved requiring multiple chemical estimations on a single strip. The dyeing methods are subject to the criticism that the dyes vary in their affinities for the various proteins and although the corrective factors may be applied for the normal proteins there is no way in

FIG. 3



Two cases of hypoproteinemia. The upper two strips are from a case of nutritional hypoproteinemia; the first strip shows a general depletion of all components while the second shows the return to normal after six weeks of dietary therapy.

translating these corrections to pathologic proteins whose dye affinities are unknown. Furthermore, various dyes and various batches of a specific dye may show considerable variation in staining characteristics. Other variations may occur in technical procedure. The scanning technic, while it is certainly the most convenient, is subject to the variations in dye affinity and in addition to light scattering which occurs when light is transmitted through the fine mesh cellulose fibres which comprise the filter paper. The size of the fibres, the fineness of the mesh, the thickness of the paper, and the distance of the slit from the paper and light source are variable factors.

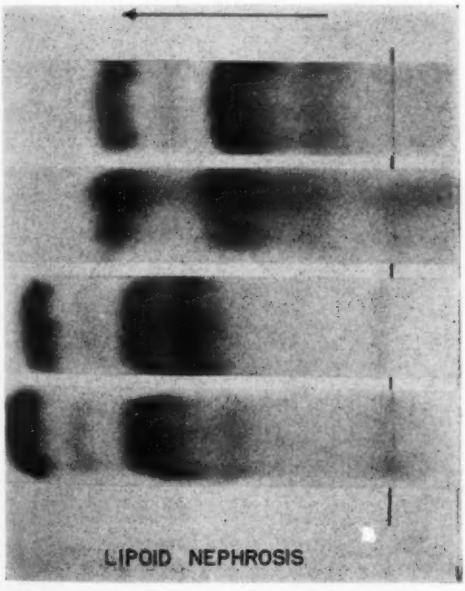
Fortunately, it is possible to secure much evidence of clinical value by a visual scanning of the filter paper without the use of involved and expensive apparatuses whose results are of doubtful significance and accuracy.

The present review is designed to illustrate the type of information which is available and to suggest further areas in which accumulation of data may be valuable.

Idiopathic Hypoproteinemias

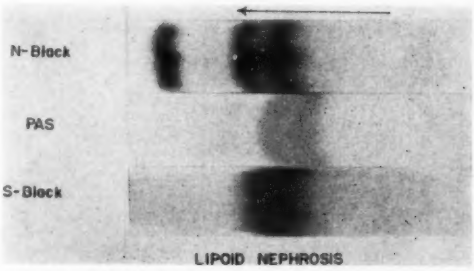
Recent observations of agammaglobulinemia[3] and the occurrence of "immunological paralysis" has led to an increased interest in these peculiar conditions. Primary agammaglobulinemia may occur in children or adults and may be acquired or congenital. It is believed to be due to a defect in specific protein synthesis and is frequently associated with lack of plasma cells or defects in activity of the germinal centers of lymph nodes. The development of filter paper electrophoresis has made recognition of this condition fairly easy and there is a rapidly developing literature of case reports on this subject. These individuals almost always show some degree of "immunological paralysis" with inability to produce specific or natural blood group antibodies. Filter paper electrophoresis is indicated in all types of recurrent infection and in such conditions as bronchiectasis in which there may have been an infection in the background.

FIG. 4



Four cases of lipoid nephrosis showing low to absent gamma globulins, lowered albumin and a marked increase in alpha$_2$ globulin in all cases. (The two lower strips were made at summer room temperature, and the proteins have migrated farther.)

FIG. 5

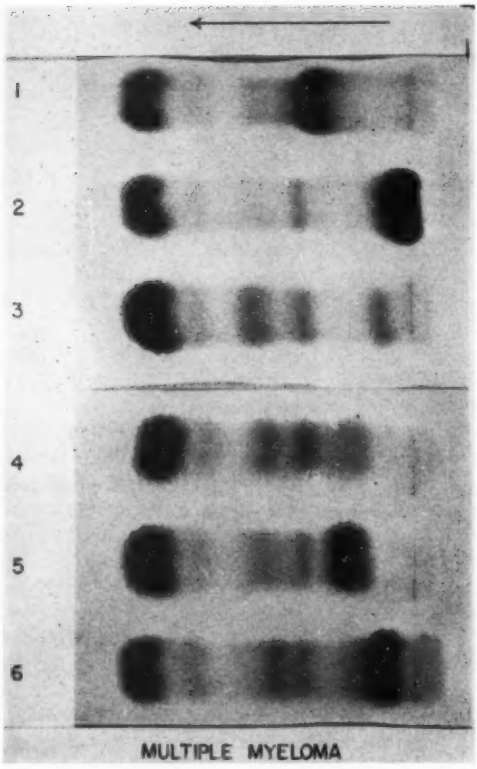


A case of lipoid nephrosis with three duplicate strips stained by naphthalene black for protein, by McManus-Hotchkiss stain for polysaccharide and by Sudan black for lipoid. The high lipoid and polysaccharide content of the abnormally increased alpha$_2$ and beta globulin is apparent.

Primary agammaglobulinemia must be distinguished from idiopathic hypoproteinemia in which there is also an unexplained deficiency in gamma globulin. However, in these latter cases there is also a concurrent decrease in albumin. The condition is probably due to an excessive catabolism and shows a protein pattern essentially similar to that seen in lipoid nephrosis, although there is no proteinuria (Fig. 3).

These idiopathic conditions must also be distinguished from secondary hypoproteinemias with agammaglobulinemia. The most important of these latter are lipoid nephrosis, nutritional hypoproteinemia and multiple myeloma. Protein patterns from two illustrative cases are shown (Fig. 3). In one instance an agammaglobulinemia in a young child

FIG. 6



Six cases of multiple myeloma. Cases 1, 3, 4 and 5 show low to absent gamma globulins. Abnormal paraproteins having variable movement are illustrated. Cases 3 and 4 showed a normal A/G ratio by salting out technic but the distinct mass of paraprotein can be seen between gamma and beta positions in each instance.

showed a marked response to nutritional therapy and a pattern six weeks after the initial electrophoresis indicates a return to normal. In the second instance a 7 year old boy showed agammaglobulinemia which was also associated with hypoalbuminemia. This case was the subject of an intensive study which indicated an excessive rate of protein catabolism involving the gamma globulin and albumin. This is the subject of a more detailed report.[25]

Secondary agammaglobulinemias are illustrated in the patterns of nephrosis (Fig. 4) and of myelomas (Figs. 6 and 7).

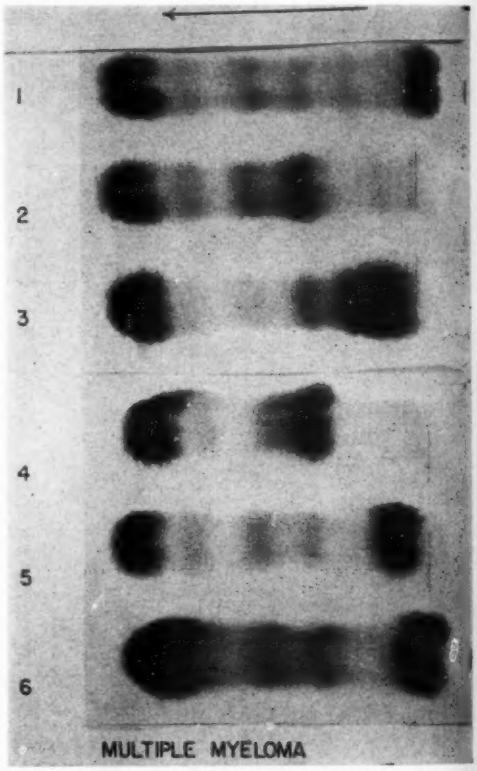
Multiple Myeloma

The use of filter paper electrophoresis has proved particularly valuable in studies of serum in myeloma. The reversed A/G ratios, hyperglobulinemia, occurrence of Bence Jones protein have long drawn attention to the importance of serum protein studies in this disease. Filter paper electrophoresis has made it feasible to study the patterns of large numbers of serums and there are now many such reports all confirming that there is an abnormal globulin which sometimes occupies the gamma, beta or alpha positions or on occasion occupies intermediate situations. For these and other reasons[22, 24, 26] it is concluded that the myeloma globulins are abnormal globulins, having a variable relationship to the normal globulins whose site on the filter paper they happen to occupy.

Twelve representative patterns selected from 24 proven cases of multiple myeloma are shown in figures 6 and 7. A number of points are worthy of attention:

1. In two cases (Figs. 6, 3, and 4) an ab-

FIG. 7



Six cases of multiple myeloma. The variable movement of the myeloma protein is illustrated. Cases 2 and 4 show secondary agammaglobulinemia. Case 1 shows two abnormal fractions.

normal component is demonstrated in the presence of a normal A/G ratio. Only by electrophoresis can fractions such as these be readily uncovered.

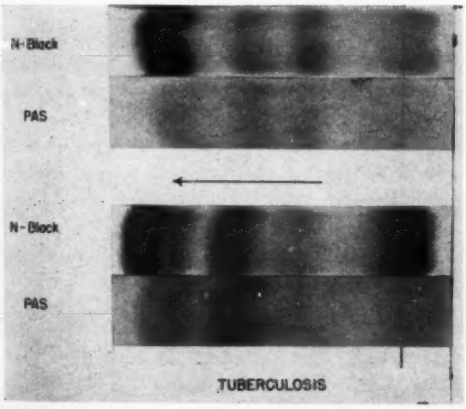
2. Many of the cases in which there has been some migration of the abnormal globulin show a deficiency of normal gamma globulin. This secondary agammaglobulinemia is probably directly related to the known ineffectiveness of antibody formation in this disease.[13]

3. In some instances there is a further dysproteinemia with an increase in alpha$_2$ globulin. Since this fraction is also increased in nephrosis this may be an indication of the peculiar type of nephrosis found in myeloma. Further correlation is required to finally establish this hypothesis.[23]

4. The myeloma protein in most instances produces a large, distinct, well demarcated mass in the filter paper. This is in distinction to the diffuse increases in normal gamma globulins which are seen in hypersensitivity (Fig. 9) and chronic hepatic disease (Fig. 10). Such concentration indicates a narrow range in the isoelectric point of the abnormal globulin and a homogeneity not found in normal gamma globulins which probably consist of several components having a common range of isoelectric points.

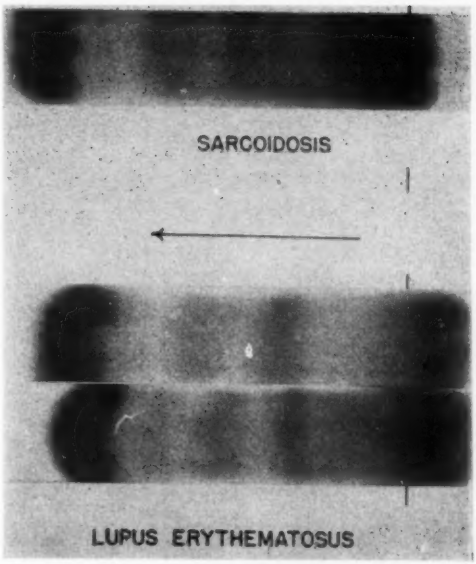
5. Two cases of myeloma, clinically unsuspected, were discovered in routine electrophoretic screening of all cases of reversal of A/G ratio.

FIG. 8



Two cases of active tuberculosis. Duplicate strips have been treated respectively with naphthalene black and the McManus-Hotchkiss procedure. The lower strip especially shows the high gamma globulin and high alpha$_2$ globulin. The latter is associated with increase in its polysaccharide-bearing component.

FIG. 9



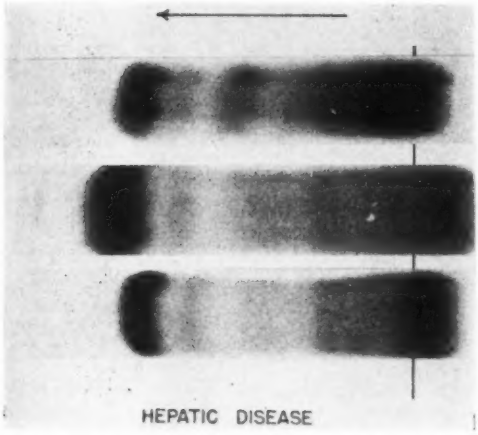
Three cases of hypersensitivity all showing the rise in normal gamma globulin. The diffuse rise which has occurred in sarcoid is also seen in chronic progressive liver disease.

Nephrosis

Chronic glomerulonephrosis or chronic (type II) nephritis with massive proteinuria show unusual features in serum protein patterns. Characteristically there is a severe depletion of the albumin and of the gamma globulin which is often almost completely absent. In association with these changes there is a rise in alpha$_2$ globulins[27, 28] which come to form the most prominent part of the serum proteins in the severe cases (Fig. 5). This increase can be shown on duplicate filter paper strips to be associated with an increase in polysaccharide content and in lipoproteins occupying the identical position of the high alpha$_2$ globulin. In one of our cases aleration of the isoelectric point of the beta globulin has produced an apparent double fraction in the alpha$_2$ position.

These findings, similar to those seen in idiopathic hypoproteinemia, indicate a selective loss of albumin and gamma globulin. The explanation of protein depletion on a basis of excessive loss by glomerular filtration alone becomes untenable, unless there is a selective loss or a compensatory increase in some components. This has led to the revival of the concept of excessive selective protein catabo-

FIG. 10



Three cases of cirrhosis of the liver. All three show a diffuse rise in the gamma globulin. Albumin seems to be low, but the alpha$_2$ globulin is unaltered.

lism in these cases. (It is also possible that the reabsorptive capacity of the renal tubular epithelium is selectively damaged, and only the ability to reabsorb alpha$_2$ and beta globulins is retained.)

Filter paper electrophoresis provides a useful clinical method assisting in the diagnosis of lipoid nephrosis and aiding in the assessment of the natural history of the disease and the effects of therapy.

The procedure is useful in the chronic renal diseases of adults including Kimmelstiel-Wilson's disease, chronic pyelonephritis and nephrosclerosis. Our preliminary investigations suggest that the changes seen in filter paper protein patterns in these conditions are probably nonspecific. The changes require extensive correlative studies with the natural history of the diseases and with the pathological lesions found at autopsy.

Hypersensitivity States

The normal response to infection is a rise in antibody titres, both specific and nonspecific. This is accompanied by a rise in gamma globulins which contain most, if not all, the specific antibodies. A similar increase occurs in diseases which fall into the class of hypersensitivities such as lupus erythematosus disseminata, rheumatic fever and rheumatoid arthritis. There is a rise in the gamma globulins (Fig. 9). This is diffuse in nature in contradistinction to the paraproteins of myeloma.

In Boeck's sarcoid which is frequently associated with hyperglobulinemia the rise is even more diffuse. This disease is believed to represent an atypical or hyperactive reticuloendothelial response to a variety of infectious agents.

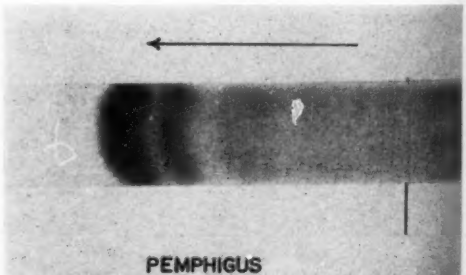
Active tuberculosis (Fig. 10) shows a similar rise in gamma globulins. This is often associated with a concurrent rise in the alpha$_2$ globulins.[10] The exact role of alpha$_2$ globulins and the relationship to hypersensitivity, susceptibility and the activity of tuberculosis require the correlation of further data.

Chronic Hepatic Disease

This shows a diffuse rise in the gamma globulins which sometimes fuse with the beta globulins. The rise is frequently associated with a splitting so that the gamma globulins may be divided into gamma$_1$ and gamma$_2$ fractions. These findings have been most apparent in cirrhosis in our studies. It is of interest to note that despite the increases in gamma globulins these are more rapidly catabolized in this disease.[6] On the other hand acute hepatitis has shown variable patterns more closely resembling the normal. Occasional transient splitting of the gamma fraction associated with a positive cephalin-cholesterol flocculation test have been noted. Transient depletion of gamma globulin was noted in one anicteric case in which previous serum protein patterns were available for study.

Zone electrophoresis provides only minor help in the diagnosis of chronic hepatic disease, but should prove valuable in assessing

FIG. 11



A case of pemphigus. This shows a rise in the alpha$_2$ globulin. The other globulins are faint or absent.

the natural history and progress of the progressive disease.

Pemphigus

An unusual pattern in a fatal case of pemphigus folliaceous is presented. This shows lowered globulins in the alpha$_2$, beta and gamma position, and a lowered albumin. These may be explained by excessive loss of serum in extensive exudation over the affected surfaces. The occurrence of a marked rise in the alpha$_1$ globulin is unique and is not readily explainable. Electrophoretic studies on the dermatoses should prove a fruitful field for investigation by this technic.

Discussion

Köiw, et al.[11] and later Cooper[4] have drawn attention to the fact that filter paper electrophoresis is a useful tool in the clinical assessment of alterations in the pattern of the serum proteins. Although it seldom provides an absolute diagnosis except in cases of primary agammaglobulinemia, it is an especially valuable adjunct in the diagnosis of multiple myeloma, nephrosis and the various hypoproteinemias.

In multiple myeloma the diagnosis can only be established by discovery of the neoplastic cells, usually in a bone marrow aspiration biopsy. Nevertheless, the occurrence of atypical fractions as we have illustrated has on occasion led to the necessary further investigations. Occasionally myeloma exists in the presence of normal albumin/globulin ratios. In these cases filter electrophoresis has shown a small but distinct abnormal globulin (Fig. 6). The procedure is particularly useful therefore as a screen to indicate whether more intensive efforts are required to establish the diagnosis of multiple myeloma.

The hypoproteinemia of lipoid nephrosis reveals a highly characteristic pattern. The progress of the disease and its severity can be assessed by the use of serial studies by filter paper electrophoresis. The factors which produce the changes in this condition are still hypothetical, but the method of zone electrophoresis provides a ready means of demonstrating the peculiar elevation of alpha$_2$ globulin associated with depletion of albumin and a secondary agammaglobulinemia. Stains with lipophilic substances such as Oil Red O or Sudan black provide a useful means of assessing the liproprotein content. These procedures are also indicated in adult renal diseases and in the glomerulonephrosis of diabetes.

Summary

1. Zone electrophoresis on filter paper may be a useful method in the clinical assessment and diagnosis of alterations in the serum proteins.

2. Quantitation by elaborate scanning methods is unnecessary since adequate information is available from visual examination of stained strips.

3. The method is adaptable to the average clinical pathology laboratory and should be used as a screen technic in all cases with alteration of the A/G ratio.

4. Agammaglobulinemia and hypoproteinemia may be diagnosed by this technic.

5. Multiple myeloma consistently shows the occurrence of abnormal globulin components (paraproteinemia). With the exception of the rare instances of Waldenström's macroglobulinemia the occurrence of such abnormal components may be considered as presumptive evidence of myeloma. The diagnosis may then be confirmed by aspiration biopsy.

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Results of Triple Arthrodesis for Rigid (Spastic) Flat Feet*

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The authors discuss the definition, pathogenesis and management of this painful orthopedic condition.

THE "SPASTIC FLAT FOOT" has long been accepted as a clinical entity, but the pathologic changes and criteria for diagnosis are still subjects for argument. In reviewing the literature, one discovers that even the misleading title is a misnomer, since many authors contend that there is neither true "spasm" of the muscles nor is the foot always "flat." The term has been applied indiscriminately so often that a more precise nomenclature and symptomatology might be adopted. This diagnosis should be reserved for the painful, rigid, pronated foot with tightness or "shortening" of the evertor group of muscles with or without recognizable bone abnormality and, in most instances, a foot which is resistant to conservative therapy. The literature does not indicate specifically the results obtained following surgical treatment and subsequent follow-up, although it has been pointed out by several authors that "conservative" or nonoperative treatment has not been satisfactory, particularly when a tarsal anomaly exists.

This report will cover the pertinent details of etiology, diagnosis, and results of treatment of the feet which have been catalogued as "spastic flat foot" and which have been operated upon at Duke Hospital during the years 1942-1954.

Etiology

Table 1 summarizes the theories of etiology of the rigid flat foot, excluding congenital anatomic tarsal defects, that have been advanced as the cause of this disabling deformity. These are rarely the actual cause for this foot deformity.

Certain authors believe the deformity to be the result of primary "irritation" to the peroneal muscles and/or nerve with subsequent peroneal muscle spasm, and eventually fixed

*Read before the Section on Orthopedic and Traumatic Surgery, Southern Medical Association, Forty-Eighth Annual Meeting, St. Louis, Mo., November 8-11, 1954.

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TABLE 1

THEORETICAL ETIOLOGY OF RIGID FLAT FOOT EXCLUDING TARSAL ANOMALIES

1. Peroneal nerve "irritation"
2. Peroneal muscle "irritation"
3. Talocalcaneal ligament "irritation"
4. "Occupation strain"
5. Trauma (indirect)
6. Infection (tonsils, etc.).
7. Specific infection (tuberculosis, osteomyelitis)
8. Rheumatoid disease

eversion of the foot. Others have maintained that sepsis, either local or in a distant focus, might play a role. Infection in the tonsillar area has been blamed in particular and has accounted for the nickname "tonsil flat foot."[1] The case histories reviewed for this study produced no evidence that infection is a specific cause of the typical rigid or "spastic flat foot."

Lapidus[2] in 1946 expressed the opinion that there may be a "lesion" in the interosseous talocalcaneal ligament or the subtalar joint itself. In a review of the anatomy of the subtalar region, he stressed the fact that the interosseous ligament which is located entirely on the fibular side of the joint becomes tense on inversion and is relaxed on eversion. He believed that with an "irritation" in this region, the evertors became "spastic" and pull the foot into pronation which is the "relaxed" position. Todd[1] stated that certain feet succumb to the effects of habitual overstrain because they are structurally and developmentally weak. Interestingly enough, a majority of the patients examined in this group had varying degrees of congenital pes planus as evidenced by the appearance of the uninvolved foot or by history prior to the onset of "spastic" foot symptoms. Trauma and occupational strain are of questionable importance, but these factors were noted frequently in the histories of the patients reviewed. Approximately one-third of the patients related the onset of symptoms to a minor injury of the foot or ankle.

TABLE 2

TARSAL ANOMALIES CAUSING RIGID FLAT FOOT

1. Calcaneonavicular bar	1921
(a) Complete	1927
(b) Incomplete	1946
2. Talocalcaneal bridge (medial)	1946
3. Sustentacular ledge	1953
4. Subtalar synostosis-complete	
5. Talocalcaneal bridge (posterior)	
6. Calcaneocuboid bridge (complete-incomplete)	
7. Other secondary ossification centers and congenital defects	

The known causes of rigid or "spastic flat foot" are listed in table 2.

Sloman[3] in 1921 and Badgley[4] in 1927 described the association of the "spastic" flat foot with a congenital osseous bar or a coalition between the anterior calcaneus and the navicular. In 1948, Harris and Beath[5] described a similar anomaly existing between the talus and calcaneus in 12 out of 17 patients whose feet were treated surgically. Webster and Roberts[6] in a report from the North Carolina Orthopaedic Hospital considered tarsal anomalies to be the most frequent cause of "spastic" flat foot and found such anomalies in 14 out of 21 patients. Harris[5] has recently described a projection of bone in the region of the sustentaculum tali which he believes to be another cause of the rigid flat

FIG. 1

(Top) Bone spurs at the periphery of the talonavicular joint and narrowing of the joint suggesting the presence of a congenital anomaly of the tarsal bones. This foot had a calcaneonavicular pseudoarthrosis. (Bottom) Opposite foot for comparison,—no abnormality.

foot. Outland and Murphy[9] described a calcaneocuboid bar as well as a posterior talocalcaneal fibrous union or fusion associated with the os trigonum resulting in a rigid flat foot. At surgery, the joint surfaces were irregular and there was limited motion in the subtalar joint. Only 5 of the 20 feet under discussion were found to have "bars" or "bridges" after x-ray examination and surgery. There were two talocalcaneal bridges, one complete fusion of the subtalar joint, one solid calcaneonavicular bar and one calcaneonavicular bar with pseudarthrosis. Six other feet showed considerable hypertrophic changes (Fig. 1, top) with spur formation and varying degrees of narrowing of the joint spaces. One foot was described at surgery as having a bony ridge about the neck of the talus. Several showed this on the roentgenogram. In the remaining 11 feet, no congenital or other specific chondro-osseous abnormalities were demonstrated, although it should be added that multiple view roentgenogram studies were not available in 6 of these.

In the final analysis, there is one group of rigid flat feet with specific tarsal anomalies. These feet usually require a triple arthrodesis in order to relieve symptoms and correct deformity. Occasionally, excision of a talonavicular "bar" at age 9 or 10 may increase the range of motion and may prevent pain. The "bar" may regenerate with recurrence of symptoms and a triple arthrodesis may have to be done at a later time.

There is a second group of rigid feet with known etiology such as tenosynovitis, rheumatoid arthritis or specific infection of one bone or joint, resulting in a rigid flat foot which may respond to specific treatment of the particular disease present.

There is a third group with no recognizable cause.

Symptoms, Signs, and Diagnosis

The group under study was equally divided between male and female, white and colored. The majority of the patients were adolescent with an average age of 16, but age ranged from a low of 9 years to a high of 54 years. The average duration of specific symptoms prior to surgery was two years.

In the 9 year old patient, occasional complaints of foot pain had been present since age 6. Since ossification of tarsal anomalies is usually not completed until age 9, roentgen study done earlier may not show a "bar" or "bridge" although clinically there may be limited subtalar motion.

Table 3 summarizes the usual signs and symptoms which accompany the rigid flat foot.

Pain was the most common presenting symptom and was usually localized to the subtalar joint either laterally or medially. A few patients located the pain in the region of the talonavicular joint; others indicated that the pain was diffuse over the tarsal area. The symptom of pain was usually precipitated by prolonged weight bearing and relieved by rest. Limited motion in the tarsal joints and swelling about the long arch were common symptoms. The severity of the complaints varied. The records show that the examiners were frequently impressed with the rigidity of the foot particularly in the subtalar joint. Forced inversion of the foot caused joint pain and prominence of the "tight" peroneal tendons. The word "spasm" was used liberally in describing the condition of the peroneal muscles. This finding may be present in the long toe extensor as well as in the peroneal muscles.[2] But there is no proof that a "spasm" or tetanic contraction of the peroneal or extensor muscle actually occurs in the foot with an anatomic defect. Harris and Beth[5] have stated specifically that electromyographic studies reveal no true spasm, but as a result of the prolonged eversion organic shortening of the muscles has occurred. Studies of muscle fiber length have not been reported. There may be active contraction of the evertor muscles in the foot which has been injured or which has active infection causing the "spasticity." The medial longitudinal arch was altered in most cases and described as "flattened." The status of the heel cord and all muscles was difficult to evaluate because of pain and fixed eversion

TABLE 3

RIGID FLAT FEET

Symptoms	
1.	"Pain above heel"
2.	"Pain middle of foot"
3.	Long arch swelling
4.	"Stiff foot"
Signs	
1.	Limited inversion-pain
2.	"Tight peroneals and toe extensors"
3.	Long arch depressed
4.	Pain over sustentaculum
5.	Pain in sinus tarsi

of the foot. Roberts and Webster[6] have pointed out that in cases of a talocalcaneal bridge, palpation of the foot may reveal a fullness posterior and inferior to the medial malleolus.

Roentgenogram Technic. The existence of tarsal abnormalities was not appreciated for many years because they are not always apparent on routine roentgenograms of the foot. The four projections of the foot necessary to detect bony abnormalities include anterior-posterior, lateral, lateral oblique at 45 degrees, and posterior oblique at 45 degrees (axial view)[5, 6, 7]. If a complete calcaneonavicular coalition is noted on the oblique roentgenogram, the anterior view will show lateral deviation of the navicular bone when compared to the neutral position on the normal side. The posterior oblique roentgenogram will reveal any union, complete or partial, between the talus and calcaneus medially. This view may also show an overhanging ledge from the sustentaculum tali which would prevent smooth gliding of this joint. Another roentgen finding seen frequently is the osteophytic "lipping" along the dorsolateral margin of the talonavicular joint. According to Harris and Beath,[5] such "lipping" in the "spastic" foot is usually associated with incongruity of the tarsal joints which limits movement in the subtalar joint thus distorting talonavicular motion. The roentgen projection and positioning of the foot must be accurate or misinterpretation will result.

Treatment

During the last 40 years, great variation in treatment of the rigid flat foot indicates that no single procedure or combination of procedures has led to uniformly good results. Since specific causes of the rigid foot were not recognized, numerous methods of treatment were tried. Todd stated that the mainstay of treatment was complete physiologic rest. He believed that he achieved this by the application of a short leg cast with the foot in neutral position. He warned against holding the foot in the over-corrected position, which might result in increased "spasm" of the peroneal muscles. His patients were instructed to bear no weight, and the cast to remain on the foot for six weeks. Weight bearing without the cast was then cautiously resumed. He gives no follow-up statistics. The use of heat, warm soaks, whirlpool baths, and inside wedges on the sole and heel of the shoe are believed by some to be of benefit. Manipulation of the foot under anesthesia, usually followed by the application of a cast, has been widely recommended.[5] End results following these procedures are not available for analysis. Other authors oppose these measures, particularly if tarsal anomalies are present. Lapidus[2] found expertly fitted Shaffer type metal plates extremely useful for these patients. He believes that a cast mold must be made of the foot to insure a perfect fit. He mentions the prejudice against the use of a "rigid sole with a rigid foot," but he adds that the reverse conclusion was reached in his experience.

The procedures of crushing, injecting and freezing of the peroneal and sural nerves have been described for relieving peroneal spasm.[2] Lengthening or actual tenotomy of the evertor muscles have also been suggested. These methods, directed at the resulting disease rather than at the cause of the deformity, are now generally agreed to be undesirable. Roberts and Webster[6] believe that conservative therapy should be reserved for feet with tarsal anomalies in patients with occasional complaints following trauma, and for feet not mature enough for arthrodesis.

The two surgical procedures most widely accepted for treatment of the rigid, painful, flat foot are local excision of the anomalous bar, and triple arthrodesis. Excision of the bar has been reserved for young patients (age 9-12) whose feet show no evidence of arthritic change. Triple arthrodesis, although considered a radical procedure, may offer the best end result when irreversible changes exist. Crego and Ford[8] have reported results of the surgical treatment in 111 cases of flat feet in children, including 17 cases of the "spastic" variety. They have concluded that although the earlier procedures of arthrodesing the talonavicular and naviculocuneiform joints were fairly satisfactory, the results were better in treatment of the painful flat foot when the subtalar joint was included. Harris and Beath[5] found that in the older age group the only surgical procedure of value was arthrodesis of subtalar and talonavicular joints. This would imply that the "bar" and "bridge" cause pain due to limitation of subtalar motion.

This survey includes only those rigid painful feet which were subsequently operated upon. There is a total of 19 patients, four of whom had bilateral foot deformities, giving a total of 23 feet for review. Seven of these patients received "conservative" therapy over a period ranging from three months to two years with the treatment consisting of manipulation, whirlpool, plaster immobilization, peroneal and sural nerve block, and in two cases, tenotomy of the peroneal tendons. In general, all seven were resistant to this kind of treatment, and none were relieved of pain for any appreciable time.

Twenty of the 23 feet in this group were treated by triple arthrodesis using the principles described by Hoke. In addition to the usual lateral incision, a second medial incision was used in several instances particularly if there was talocalcaneal disease. The cartilage and bone were removed in the manner employed when correcting a valgus foot. An effort was made to observe any abnormal bone formation or congenital fusion involving the talus, navicular, or calcaneus. One patient had complete congenital fusion between calcaneus and talus (bilateral), and required only arthrodesis of the calcaneocuboid and talonavicular joints of one foot (Fig. 2). Prior to operation, this patient had mid-foot pain which prevented him from working as a machine repairman. Following operation, he returned to work. The opposite foot untreated by operation is now uncomfortable at times and is being supported by a Whitman plate. Note the spurs present at the talonavicular joint.

FIG. 2

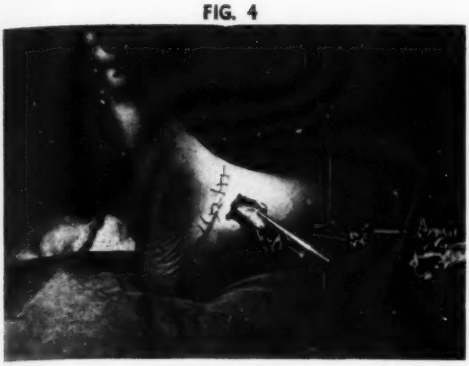
Lateral and oblique roentgenograms showing complete synostosis between talus and calcaneus. Notice the reaction at talonavicular joint.

FIG. 3

Foot on right is a rigid flat foot due to calcaneonavicular bar. Active and passive inversion is limited; pain occurs with weight bearing.

Of the three feet which did not have the Hoke arthrodesis, a local excision of the anomalous tarsal bar was performed in two and a Miller flat foot plastic procedure in the other. The Miller procedure is not indicated in this type of foot,[8] because the operation does not include the subtalar joint and allows continued eversion and motion. Simple excision of the "bar" was done in a 12 year old boy whose foot showed no evidence of arthritic change in the joints. This operation was done two years ago, and up to the present time the result has been satisfactory. The "bar" excision was also done in a 12 year old white boy approximately one year ago (Fig. 3-4). He notices less pain than he had prior to operation, but he does have aching in the afternoon after walking all day. The limitation of inversion and eversion was as much postoperatively as it was preoperatively. The foot mo-

FIG. 4



Same foot as in figure 3 at operation after "bar" has been excised. Range of motion improved slightly and pain diminished.

tion now is no greater than if a triple arthrodesis had been done.

If the foot in a young child shows minimal valgus deformity, moderate limitation of motion, and no degenerative joint change, excision of the bar is indicated. Increase in range of motion and relief of pain may occur. Triple arthrodesis can be done later if pain recurs.

The criteria for analysis of the feet following triple arthrodesis were: (1) relief of pain and fatigue, (2) daily function of the foot, and (3) anatomic alignment. A foot was classified in group A if it was not painful, if it caused no limitation of activity, and if the appearance was good. A group B classification indicated improvement over the preoperative condition with minimal ache and some limitation of the patients' activities. Group C was reserved for those in which pain and deformity persisted. Table 4 indicates the condition of the feet following operation.

Eight of the 20 feet on which triple arthrodesis has been done were classified in group A, 9 in group B, and one in group C. Two patients who had a triple arthrodesis had insufficient follow-up. One colored male in group A had bilateral arthrodesis five years ago. He stated, at the time of a recent examination, that he was plowing all day without discomfort. The single foot classified as group C (poor) showed recurrence of eversion deformity and moderate discomfort on weight bearing. It should be mentioned, however, that the patient stated he was improved by surgery.

TABLE 4

RESULTS FOLLOWING TRIPLE ARTHRODESIS IN 20 RIGID PAINFUL FLAT FEET

Group A	8
Group B	9
Group C	1
Insufficient follow-up	2

Conclusions

(1) A more precise nomenclature should be adopted to designate this clinical entity; that is, rigid flat foot due to congenital bar, etc.

(2) The etiology of rigid flat foot may frequently be determined. Specific factors have been observed and any one of these may produce the everted flat foot as: (a) calcaneonavicular bar; (b) talocalcaneal bridge (medial); (c) no obvious synostosis, but possibly a pseudarthrosis at either A or B; (d) overhanging ledge in the region of the sustentaculum tali with hypertrophic changes between the talus and navicular; (e) subtalar synostosis, partial or complete; (f) calcaneocuboid bridge; (g) recognized trauma, rheumatoid arthritis, or specific infection may cause the foot to assume the same rigid valgus position.

(3) Foot pain and rigidity plus shortening of the peroneal muscles are the most frequent clinical findings. Multiview roentgenograms are important in order to demonstrate tarsal anomalies. Ossification of the cartilage which is a precursor of the bar, bridge, or synostosis, usually does not occur until age 9.

(4) Conservative treatment should be reserved for young children or for those individuals with occasional symptoms. Local excision to an anomalous tarsal bar is indicated only in the younger age group (9 to 13 years) with no arthritic change in the joints.

(5) A triple arthrodesis as treatment for this type of foot results in a serviceable foot which occasionally may be uncomfortable but which is satisfactory for function.

(6) All patients in this group, regardless of specific classification of end results, had improvement in foot function and diminution of pain following triple arthrodesis.

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Discussion (Abstract)

Dr. Relton McCarroll, St. Louis, Mo. The spastic, rigid, painful flat foot does not have to be the result of a developmental defect in the bony structure of the foot itself. This condition may occur secondary to other abnormalities in the foot, may occur secondary to injury, infection, and other developmental defects in the structural make-up of the foot itself.

It may also occur in conjunction with Kohler's disease, which is occasionally reported. It may follow osteochondritis dissecans within the ankle joint. In the majority of instances, however, these other abnormalities can be proven by x-ray studies, aided of course, in the presence of an infection or a traumatic condition, by an adequate history and an adequate physical examination. In those instances in which the etiology is not obvious on the basis of examination and x-ray studies, one must consider the possibility of some developmental defect in the bony structure of the hind foot.

Drs. Musgrave and Goldner have stated that only four of their 22 cases showed evidence of a bony abnormality on x-ray examination or on observations made at the time of operation. This does not mean a thing because it is often impossible to prove the presence of this condition on any examination either by physical examination or x-ray studies. The presence of a bar in the calcaneo-navicular region is not difficult to identify or establish as a definite diagnosis, because you can usually show this in the ordinary oblique views of the foot. But in those abnormalities that occur in the talocaneal region, it is difficult or impossible at times to show them on x-ray studies.

We saw one film here today in which it was impossible to see any evidence of abnormality, in fact, very little in the way of bone changes around the sustentaculum tali on each side, and that is not an uncommon finding, at least in my experience.

They also showed us another example in which you had a complete fusion of the talus and calcaneus on one side, in the region of the sustentaculum, while on the other side the joint was well established and open. In a unilateral involvement, this means something, but in a bilateral involvement, in which there is no fusion, the joint is intact, and it is almost impossible to identify any evidence of changes after adequate x-ray studies.

If, therefore, we are dealing with a foot in which we cannot establish a definite diagnosis, I think we are safe in assuming in the majority of instances that we are dealing with some abnormality in the posterior portion of this foot. I also agree that in the foot which is old enough for surgical treatment, old enough for stabilization, and in which the foot remains painful and disabling in spite of adequate conservative treatment, a triple arthrodesis represents the best approach to the problem. It must be remembered, however, that many of these feet can be controlled with conservative measures and not all of them require surgical intervention to that extent.

In closing, there is one question I would like to ask Drs. Musgrave and Goldner. We see an infant child at times about 18 months of age, or from 18 months to three years, who has all the clinical findings of this type of foot. We do not know whether it is painful or not, because these children do not often complain, but they limp, they hold the foot fixed in valgus. If it represents unilateral involvement, there is an atrophy of the calf on that side, as compared to the other, and we have difficulty inverting this foot. It can, at times, be passively inverted. I have often wondered whether or not in a child of that type we might go ahead and explore this foot and actually totally excise the sustentaculum tali from the median approach and also any associated abnormality which may be present on this side, because if we lose with this procedure we are no worse off than we were to begin with, and we have not decreased the possibility of a satisfactory result with the triple arthrodesis in later years.

I would like to ask Drs. Musgrave and Goldner whether or not they encountered this problem in children of that age, and if so, whether or not they feel that surgical intervention of this type may be justified.

Dr. Ben Fowler, Nashville, Tenn. I just have one comment to make on the problem of the calcaneonavicular bar, as in the other congenital deformities it has not a direct relationship but merely serves to weaken the general structure. Then you have the phenomenon of the spastic complication developing on top of it. I personally feel that most of these cases in their acute stage fall into the category of almost an arthrofibrosis, or even of a vasomotor dystrophy of the extremity. Very often, as you know, there will be a difference. You can have two feet both of which are flat, one of which exhibits the spastic element, and the radiograph will show if the spasticity has been of considerable duration that there is decalcification on that side. I have on two or three occasions, when I was busy and did not have time to overtreat them, had them walk out of the office with a prescription for Butazoladin and within two or three days have normal mobility return to their foot in so far as the structural elements were concerned. In other words, it would be identically mobile with the other foot. I think this is one of the best ways to measure the degree of the associated changes in the so-called spasm which is not spasm, because you can block the peroneal nerve and it does not change the motion of the foot. There is a more complex factor than that, and this is to measure the plantar flexion of the foot because the taut tensors are also involved with the peroneals. This gives you just a key as to how much involvement this is other than in the joints and is an easy thing to measure. Butazoladin and cortisone will often completely and very rapidly terminate all of the acute manifestations in the foot, and then it can usually be treated conservatively quite satisfactorily.

Dr. Goldner (closing). In the case of the man who had complete arthrodesis of both subtalar joints, he

finally developed pain on both sides with occupational strain. This is a problem, obviously, that is not completely solved by considering all of these feet as congenital abnormalities. On the other hand, we have two or three families on whom we hold clinics in which all of the children have what we refer to as rigid, painful flat feet. One child at age 2 shows them, and the mother and father both show them at age 52. They are walking on their medial malleolus, the feet are in extreme valgus, and yet they do not show any bar. These represent congenitally severe flat feet without any specific deformities. The fact that you cannot see the deformities in all the feet, does not mean that they are not there, as Dr. McCarroll has pointed out. But I believe that if they are obvious enough, one should be able to find something about them either by x-ray or at operation.

Conservative therapy has certianly helped in some feet. The feet that Dr. Fowler is talking about may fall into a third category, or they may really be what we are talking about here. Is this a congenital rigid flat foot, or is this a tali synovitis, a mild rheumatoid arthritis, or something else? Most of the ones we see have received therapy of all kinds for several months and they still have reverted to their original difficulty.

Dr. McCarroll asked about the infants. We have three two year old children now who have developed painful flat feet. One patient turned up with mild Still's disease. They do have swelling along the posterior tibial tendon, a chronic tenosynovitis. We have obtained a biopsy of their tendons, and they have thickening of their ankle joints. They do not have any bony abnormality that we can see but, obviously, in a child this age, the x-ray examination is of no help. The foot has not developed enough cartilage or bone to tell whether abnormalities are present. Maybe they represent early rigid flat feet. So far we cannot answer these questions.

Bullous Dermatoses in the Southern Negro

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This form of skin reaction, according to the authors, presents a more serious disease in the Negro than in the white race.

THE 105 HOSPITALIZED CASES of bullous dermatoses in the Negro which are the subject of this paper, were observed at Charity Hospital in New Orleans. The yearly admissions in the past were approximately equal for both races. In the last decade or more Negro admissions have steadily increased. For the five year period covered by this report, ending June 30, 1954, approximately 68 per cent of admissions were Negro. During this period there were 1,700 admissions to the dermatologic service of which 779, about 48 per cent, were Negro.

In general the health of Negroes is not as good as that of white patients. Their diet is deficient in many respects, though, dermatoses due to vitamin deficiencies are unusual probably because of the general practice of adding vitamin supplements to bread. In our opinion the background of health of the Negro makes him less favorable for recovery from dermatoses than the white patient. We believe this to be true clinically, case for case, though it is impossible to prove statistically. Though the greater amount of pigment in their skin helps to protect Negroes from the sun, they are nonetheless susceptible to photosensitizing diseases. They almost never exfoliate, though they work in the sun for long periods of time, yet such diseases as lupus erythematosus are aggravated by exposure to the sun in the Negro just as in white patients.

The Negro has an oily, seborrheic skin, which makes him particularly susceptible to various kinds of dermatitis. Acne, frequent

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in white patients, is also frequent in Negroes of mixed blood though it is seldom observed in pure black Negroes. He shows almost complete lack of resistance to pustular types of dermatitis, and many skin conditions readily diagnosed in white subjects are sometimes difficult to diagnose in Negroes because they do not present themselves until secondary pustular eruptions have altered the picture.

Bullous dermatoses are somewhat more frequent in the Negro than in the white, and are decidedly more serious, as is shown by the seven fatalities which occurred in these 105 cases. The appearance of these lesions in the Negro is much like that in white patients except that: (1) the erythema, so often a useful diagnostic feature, is not evident in Negroes, and diagnosis is sometimes delayed for this reason; and (2) many bullous dermatoses in the Negro may be described almost as "violent." The lesions are widespread, numerous and very large, and involvement of the mucous membrane occurs in a fairly high percentage of cases.

The largest groups of bullous dermatoses in this series were pemphigus (12 cases), herpes zoster (21 cases), impetigo (22 cases) and drug eruptions (33 cases). The more infrequent varieties will be briefly discussed before these are considered.

Vaccinia

Two cases of vaccinia occurred in a 14 month old child and a two year old child. The former, who had had eczema for some time, presented typical generalized lesions two weeks after contact with a sister who had just been vaccinated. The eruption cleared with only general treatment. The other child presented a typical eruption on the face and extremities three days after vaccination. A staphylococcus was cultured from the lesions which promptly disappeared under penicillin therapy. In both instances contact was clearly established and careless hygienic practices could be assumed.

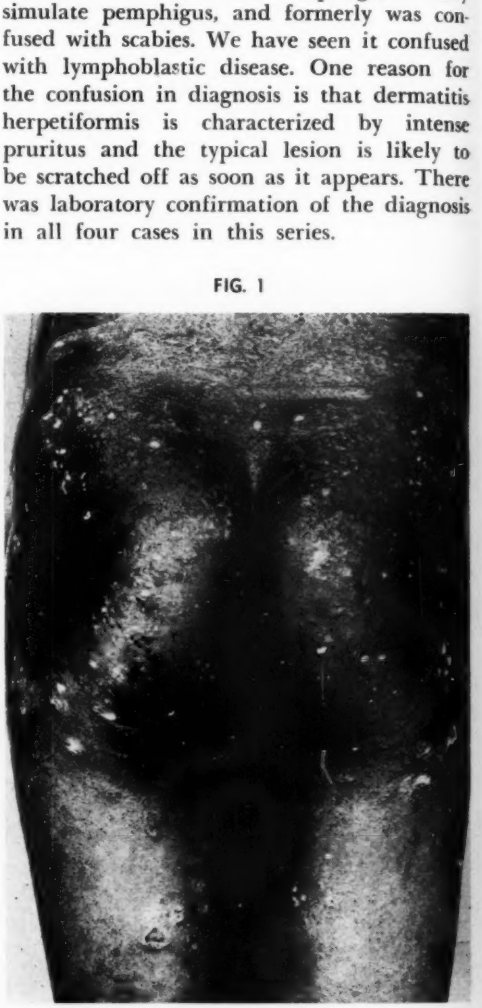
Pemphigus Erythematoses

The two cases of Senear-Usher disease in the series occurred in women aged 48 and 49 years, respectively. The lesions in each were typically those of pemphigus but the distribution was that of lupus erythematosus. Neither was seriously ill and both improved promptly without the use of steroids. (From observation of patients in private practice, we feel that patients with this disease do not respond as well to this type of therapy as do patients with pemphigus.) Tzanck cells were found in profusion in both cases, as they always are if the material for examination is obtained from fresh lesions.

Dermatitis Herpetiformis

Duhring's disease (Fig. 1), appears in the Negro in about the same frequency as in the white, though we believe the diagnosis is missed more often than it is made. It is sometimes confused with impetigo, it may simulate pemphigus, and formerly was confused with scabies. We have seen it confused with lymphoblastic disease. One reason for the confusion in diagnosis is that dermatitis herpetiformis is characterized by intense pruritus and the typical lesion is likely to be scratched off as soon as it appears. There was laboratory confirmation of the diagnosis in all four cases in this series.

FIG. 1



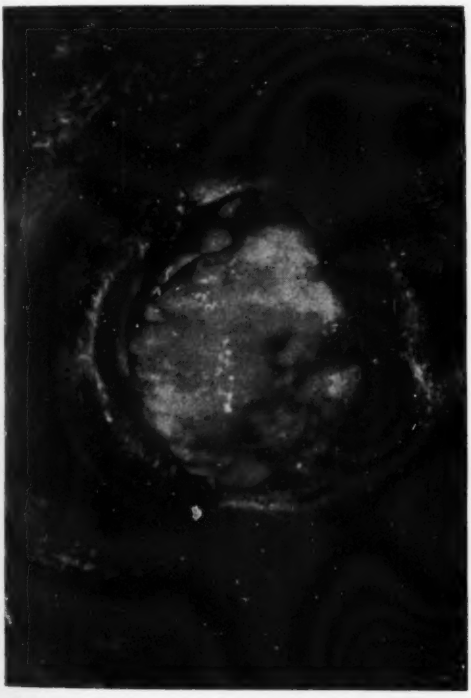
Dermatitis herpetiformis. The location is typical.

Two women, 33 and 42 years of age, respectively, had their attacks during pregnancy. The disease was mild and promptly disappeared under general measures in one case, and under sulfapyridine in the other. The other two patients were men, 21 and 68 years of age. In one the eruption was present only on the extremities, in the other it was generalized. Both vesicles and pustules were present in association with the bullae. Both patients responded promptly to sulfapyridine. In our opinion this favorable response is so characteristic of dermatitis herpetiformis that an immediate therapeutic test is justified in doubtful cases.

Erythema Multiforme

When Noojin and Callaway[1] reported 54 cases of erythema multiforme and erythema nodosum, they commented that there were no Negro cases in the group, although one of every four clinic admissions was a Negro patient. In contrast to this there were six cases of erythema multiforme in our 105 cases of bullous dermatoses.

FIG. 2



Erythema multiforme with moderately severe involvement of oral mucosa.

FIG. 3

Generalized erythema multiforme in a woman showing the iris type of lesion.

They ranged in age from 4 to 48 years. Erythema multiforme is particularly acute in its manifestations, and severe in its course in this race, and many of these patients were seriously ill. Several of them had lesions of the mucous membrane (Figs. 2 and 3). The blisters were often enormous; fever was often high. Transfusions and intensive supportive therapy were often necessary, in contrast to the larger number of patients in the clinic who can be treated on an ambulatory basis because the lesions are small and vesicular, and the patient is not seriously ill. Tzanck cells are not found in erythema multiforme.

Lupus Erythematosus

The two cases of this disease having bullous lesions were in females. An 11 year old girl had lesions on the face, neck, shoulders and anterior chest; there was no known etiologic factor. The other, a 33 year old woman, had lesions only on the extremities and posterior chest; she became ill after taking sulfona-

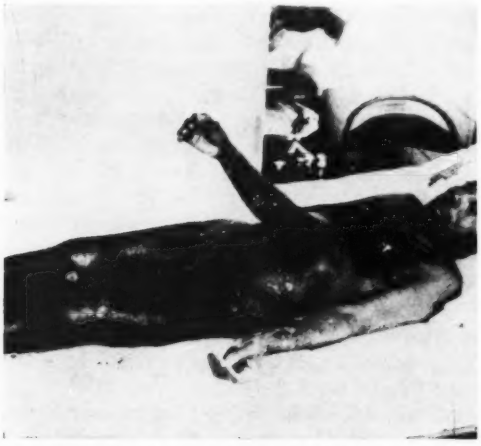
mides. In both the laboratory diagnosis was positive for lupus erythematosus. The woman responded satisfactorily to a combination of cortisone and ACTH. The girl, who had had her eruption for three months when she was first seen, has been very ill at intervals during the two year period of observation; she has had glomerulonephritis and has also presented the nephrotic syndrome. She has responded to cortisone, however, and is in fairly good condition at the present time, though she still has this disease.

Pemphigus

Negroes seem to have pemphigus later in life than white patients. The age range in the 13 cases in this series was from 19 to 82 years, but nine of the patients were 52 years old or older. The four patients who died were, respectively, 19, 42, 52 and 60 years of age. This is a disease of the lower economic levels. The high mortality, four deaths in 13 cases, bears out our impression that it is the most difficult of all dermatoses to treat in the Negro race.

Pemphigus is bizarre in its manifestations, and therefore difficult to diagnose, in both races, but more particularly in the Negro (Fig. 4). It is not unusual to have a patient come in with an apparent drug eruption which, in a day or two, looks like erythema multiforme, and finally establishes itself as pemphigus by its persistence and its failure to respond to therapy. Tzanck cells have been found in all cases in which they have been searched for, and have been found more readily, and in greater profusion, than in any other skin disease, though they are not specific for pemphigus.

FIG. 4



Generalized pemphigus of about 6 months duration in bedridden man.

The foliaceous variety of pemphigus has not been observed in Negroes at Charity Hospital. (Such an instance was observed in a 54 year old Negro at the Veterans Hospital. He cleared up under cortisone, but failing to continue this, he returned with pemphigus vulgaris, and his next relapse was into pemphigus vegetans.)

The duration of the illness in these 13 cases before the admission to the hospital varied from one month to five years. In the four fatal cases it had lasted for one month in one case, for a year in two, and in the fourth the duration was unknown. The eruption was generalized in the fatal cases and in five of the non-fatal cases. Large bullae were present in the fatal cases. In one case the rash appeared on the day penicillin was given for an upper respiratory infection; it persisted for seven weeks and eventually cleared up entirely under sulfapyridine.

One patient died of thrombophlebitis and pulmonary infarction; the adrenal glands were negative at autopsy. A second patient also died of pulmonary infarction. In the two other fatalities the cause of death is not clear. One patient was admitted shortly after he had been treated by x-ray over the liver, in an attempt to control the skin disease. It is not unusual for patients with pemphigus to die of causes that are not clear. The speculation that they die of adrenal exhaustion has much to support it, particularly the improvement in the morbidity and mortality since steroid therapy was introduced. Why even with this modern therapy, some patients continue to live is hard to explain since we have seen patients survive who were terribly emaciated. It is of interest that one patient in this series, who had been ill for three years, had a perfectly normal pregnancy after treatment.

Cortisone, ACTH or both were used in 8 of the 13 cases, including three of the fatal cases. The fourth fatal case was treated with sulfapyridine. Two patients were treated with penicillin, and the remaining patients, one of whom was 66 and the other 82, were treated only by general supportive measures.

The maximum dosage of steroids was 300 mg. in all but one case, in which the dosage was temporarily increased to 500 mg. daily. These dosages are much lower than those used in some reported series. A phychosis developed in one patient under treatment with cortisone. The moon was seen in facies in one patient treated for pemphigus.

Herpes Zoster

There may be some disagreement to the inclusion of herpes zoster as a bullous dermatosis. Since bullae are present there is no good reason why it should not be included.

There were 21 cases in this series. (One death occurred in a 16 year old boy who had lymphosarcoma, immediately after x-ray treatment over the chest.) The age range was from 2 to 80 years. The disease is supposed to be uncommon in infancy and childhood, but there were two children in the series who were two years old and two others who were eight and nine years of age, respectively.

This disease is said to appear frequently in association with leukemia. That was not true in this series nor have we ever observed the association. Other diseases, however, were present in some cases. One woman had an antecedent pneumonia. A 58 year old man had multiple myeloma. One patient had meningitis of hemophilus origin and another had meningococcic meningitis. In the latter case the eruption, which was limited to the face, appeared on the third day of hospitalization. One patient was admitted with a tentative diagnosis of poliomyelitis. Not infrequently the spinal fluid in herpes zoster is under increased pressure and shows a pleocytosis, even if there are no clinical signs of meningeal irritation. Tzanck cells are found only occasionally and with difficulty in herpes zoster.

Bilateral disease, which is extremely uncommon, did not occur in this series. In seven of the 21 cases the lesions were on the face and about the eyes; in the other 14 they were on the thorax. The disease was severe in all instances but no more so than in white subjects.

Treatment ranged from compresses and aspirin to the systemic administration of Aureomycin, to which the response was usually prompt. The single patient who received vitamin B_{12} was much worse afterward. Paralysis and persistence of herpetic pain were no more frequent than in white patients.

Impetigo

Though impetigo is frequent in both colored and white patients, it is more frequent and more serious in the Negro. Over the five year period in which these 105 cases of bullous dermatoses were collected, no white patient had impetigo of the severity to warrant hospitalization, but there were 22 Negro admissions for this cause.

It is predominantly a disease of youth, especially of infancy. The age range in our 22 cases was from prematurity to 15 years. The premature child was a newborn. Four patients were less than a year old, seven others were less than two years, and five others less than five years of age. The disease was generalized in six cases and localized to various parts of the body in the other 16.

Impetigo has a special predilection for the face, head and scalp. In Negro patients it frequently appears first inside the nose and spreads from there. Because of the special tendency toward secondary pustular eruptions in the Negro, such lesions in the dangerous areas of the face, are always of serious import. Bullous impetigo in the Negro is also often complicated by a folliculitis of the scalp, which may be very obstinate. We explain this by the fact that the hair is much tougher in this race, and the hair follicles much larger.

Negro children are peculiarly susceptible to bullous impetigo. We have observed it within an hour or two after birth, as in the premature child in this series. The eruption was not typical in all respects in this case, but the final antemortem diagnosis was impetigo. Histopathologic studies are not yet complete. The findings at autopsy included septicemia, focal abscesses of the lungs and liver, basilar meningitis, moniliasis of the oral mucosa and the esophagus, and ileus.

The most serious complication in this series was acute glomerulonephritis, which was present in five of the 22 cases, in every instance apparently secondary to the skin infection. The organisms isolated in this series were beta hemolytic streptococcus, hemolytic staphylococcus, and *Staphylococcus aureus,*

sometimes alone and sometimes in combination. All patients with streptococcic infections did not develop glomerulonephritis, but it is significant that the streptococcus was the causative agent in every case in which this complication appeared. Hypersensitivity is perhaps the explanation.

One case was managed by supportive therapy only. The premature child, who died, was treated by Terramycin and Chloromycetin. The other 19 children were treated with penicillin. It has previously been our policy to treat ambulatory patients in the clinic only with such agents as Aureomycin ointment, bacitracin ointment, or, because it is cheap, ammoniated mercury. Systemic antibiotic therapy is reserved for severe cases. In view of the high incidence of glomerulonephritis in this small series, a fact which had previously escaped us, and the risk of residual kidney damage in these children, we have already changed our policy and are ordering penicillin routinely for impetigo without regard to the severity of the infection.

Drug Eruptions

The 33 cases of drug induced dermatoses formed the largest and in many respects the most interesting group in this series. The cases fall into two sub-groups, 16 cases in which the drugs ordinarily used, or unknown drugs, were responsible, and 17 cases in which the eruption followed the use of a popular patent medicine, "666."

Most drug eruptions in white subjects take the form of urticarial and erythematous lesions, or erythema multiforme. Bullous lesions are infrequent, as is shown by the fact that over the five year period in which these 33 cases were observed in Negroes, there were only three white admissions for this cause. In these cases the eruptions followed the use of sulfathiazole, bromides, and bromoquinine, respectively.

Negroes are unusually susceptible to drugs, pure blacks more so than those of mixed blood. They present frequent reactions to hair straighteners and to bleaches. They use drugs with unusual frequency, often without any indication, and in many strange ways. They apply turpentine, mineral spirits, and a popular patent medicine, Tichenor's antiseptic, to all local lesions. When salvarsan was the standard treatment of syphilis, many Negroes were hospitalized because of serious reactions, which were always of the exfoliative type.

The Negro's reaction to drugs is frequently serious and is sometimes fatal. One of us observed a Negro given two tablets of sulfadiazine for gonorrhea, who complained immediately of malaise, was covered with gigantic blisters in 10 hours, and was dead within 24 hours. In another instance, observed at Charity Hospital, a Negro who was given a lipiodol instillation for bronchography, without preliminary testing, had a violent reaction within 10 hours and died 26 hours later. Diadrast, however, apparently causes no greater proportion of reactions in the Negro than in white subjects.

Primaquine has recently been introduced for the prevention of relapse in malaria. It should be used with great caution in Negroes. Preliminary studies have shown that while a dosage of 10 to 240 mg. daily is a safe dosage range in white adults,[2] daily doses of 30 mg. (base) are too toxic to be used in Negroes without close medical supervision.[3] Anemia, methemoglobinemia and leukopenia have been observed after large doses. The manufacturers are warning that primaquine must be used cautiously in Negroes, and we regard both the warning and the reaction as typical of the Negro response to drugs.

In the 11 cases in this series in which the nature of the drug causing the reaction was known, the dermatitis could be attributed to penicillin and sulfonamide drugs in three cases each, to barbiturates in two cases, and to salicylates, phenolphthalein and Dilantin in one case each. In the five remaining cases the patients did not know what they had been taking. The age range in these 16 cases was from 5 to 75 years.

One of the reactions to penicillin occurred in the hospital in a patient who was receiving the drug for dermatitis venenata. The reaction to phenolphthalein occurred in a patient who had the laxative habit (Fig. 5). The eruption was generalized, though one usually thinks of such lesions as localized and fixed. The reaction to Dilantin occurred in a six year old child under treatment for epilepsy. Another child of the same age had a reaction to phenobarbital; it was complicated by acute glomerulonephritis and the Stevens-Johnson syndrome. A 22 year old woman

FIG. 5

Fixed drug eruption (phenolphthalein) showing numerous bullae.

with a reaction to sulfonamide therapy also had mucous membrane lesions.

The duration in most of these cases was brief, from 7 to 37 days. Most of the patients responded promptly to withdrawal of the offending drug, though cortisone, sometimes with ACTH, was necessary in a few cases. In one instance, in which a severe dermatitis on the face and extremities followed the use of penicillin, an antihistamine and Terramycin were also employed.

"666," which was responsible for 17 cases of bullous dermatitis (Fig. 6), is a patent medicine commonly used by Negroes. It is taken for colds, constipation, as a spring tonic, a general tonic, and for no conceivable reason. It is distributed in two forms. One, a quinine preparation taken for chills and fever, causes no reactions. The other preparation contains ammonium chloride, magnesium sulfate and citric acid in innocuous amounts, and antipyrine, the offending drug, in the ratio of 10 grains to the ounce. The dose is a tablespoonful twice daily, a quantity which, unless sensitization is present, should give rise to no difficulties. Instead of measuring it, however, some patients drink it from the bottle or pour it into a glass. A 37 year old woman who did not survive took "a lot of it" for a cold. In view of the quantities and the careless way in which "666" is consumed, it is surprising that reactions to it are not more frequent.

These 17 cases are, of course, only the severe ones, in which admission to the hospital was necessary. Many milder cases are seen in the clinic. We have recently been informed that dentists are seeing a great many reactions to "666" in the form of lesions in the oral mucosa.

Reactions to "666" fall into two categories. In the first type, which lasts from four to seven days, the bullae are worse on the face, genitalia, hands and feet and in the mouth. The illness is often very severe. The second group presents the same clinical manifestations, but their illness lasts from 25 to 30

FIG. 6

Bullous eruption of Stevens-Johnson type following use of "666."

days. The patients, curiously, are not any more seriously ill than those in the first group. The course of the disease is simply longer.

Treatment consists of withdrawal of the medication, supportive measures, including blood transfusions, penicillin when it is indicated, and steroid therapy. Cortisone was used in two cases, once with ACTH, and ACTH was used alone in two other cases. In most of these patients the duration of illness before treatment was brief, which is an indication of the seriousness of the emergency.

The most difficult part of management is often persuading these patients that they must give up the medication which has produced their illness. They accept this idea with the greatest reluctance. They are far more willing to attribute the rash to anything else. Frequently the patients disregard the advice given them and continue to take "666." A number of recurrences have been observed which were no more acute than the original reaction.

Summary

Over a recent five year period 105 Negroes having bullous dermatoses of various kinds were hospitalized at the New Orleans Charity Hospital, where the clinics carry the bulk of the dermatologic load. Generally speaking, these dermatoses are somewhat more frequent and considerably more serious in Negro than in white subjects, as is indicated by the seven fatalities in this small series.

Each variety has been discussed briefly. There has been included a general discussion of the Negro's background, environment, and reaction to skin diseases.

Skin diseases in Negroes and whites differ in certain respects, which sometimes makes for diagnostic and therapeutic difficulties. However, they are fundamentally the same clinically and it would be a serious mistake to carry the racial differentiation too far.

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Anomalies of Brachial and Antebrachial Arteries of Surgical Significance

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Anatomic variations in the major arteries of the upper extremities are of sufficient frequency to be of practical interest to the surgeon.

THE RELATIVELY high frequency of abnormalities of the major arteries of the upper extremity is not too well appreciated by many physicians. Such variations can prove to be exceedingly confusing when encountered surgically. A knowledge of the types of aberrancies, the course and relationships of these vessels, and the statistical chances of encountering them should prove helpful.

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Materials

The arteries of 408 upper extremities, 249 adult and 159 fetal, were studied by gross dissection. The bodies used were predominantly Negro. Thirty-two per cent were female. The specimens were obtained during a three year period on the staff of the Tulane University Medical School and the past two years at the University of Texas Southwestern Medical School.

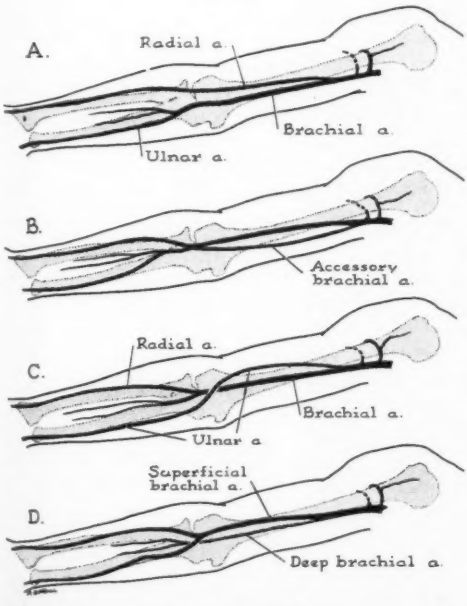
Observations

Anomalies of the three principal arteries with respect to origin or course were observed in 18.8 per cent of the specimens. A persistent median artery entered into the formation of the superficial volar arch in an additional 9 per cent. In 161 bodies both extremities were available for study. If, in addition to the three main vessels, the persistent median arteries be included, variations of similar type occurred bilaterally in 11.8 per cent. Variants occurring bilaterally but of different types were noted in 3.7 per cent. There were unilateral variations in 23.9 per cent of the specimens. In this group, 39.4 per cent of the bodies had a major variant in at least one extremity.

It was found that 34.5 per cent of the extremities from female bodies showed some type of arterial aberrance, but the frequency dropped to 24.2 per cent in a study of males. This difference was due largely to the much more frequent appearance in the female of a persistent median artery.

An abnormally high origin of the radial artery was the most frequent variation, being found in 15.6 per cent of the specimens (Figs. 1, A and 3). Quain[6] found this condition in 11 per cent, McCormack, Cauldwell, and Anson[5] in 14.27 per cent. In approximately one fourth of the current series, the radial artery originated from the anterior aspect of the axillary artery. Practically all of the remaining three fourths originated from the proximal half of the brachial artery, either the anterior or anteromedial surface.

FIG. 1



Variations in the arterial patterns shown schematically: (A) a radical artery of high origin; (B) an accessory brachial artery; (C) a high origin of the ulnar artery; (D) a superficial brachial artery.

When the radial originated from the axillary artery, the vessel passed between the medial and lateral components of the median nerve, and coursed anterior to the nerve and medial to the biceps muscle throughout the arm. In those cases in which the artery originated after formation of the median nerve, the vessel passed medial to the nerve to attain an anterior position, thereafter following the same course as those arteries of higher origin.

In 31 per cent of the radial arteries of high origin, there was an anastomotic connection of variable size in the antecubital fossa between this vessel and the ulnar artery. McCormack et al[5] found this condition in 20 per cent of their specimens. When the connection was large, the part of the radial in the brachium was of small caliber. The communicating vessel usually passed anterior to the tendon of the biceps muscle. Except for this important connection the radial artery assumed much the same relationship and connections in the forearm as did a normal vessel.

The ulnar artery originated proximal to the intercondylar line in 1.2 per cent of the extremities (Figs. 1, C and 2). This condition was reported in 2.26 per cent of McCormack's series and 0.7 per cent in the study by Adachi.[1] This unusual vessel arose from the anterior or anteromedial aspect of the proximal part of the brachial or the distal part of the axillary arteries. It coursed anterior to the median nerve and medial to the biceps muscle. In the distal third of the arm, it assumed a position medial to the median nerve and entered the forearm in this relationship.

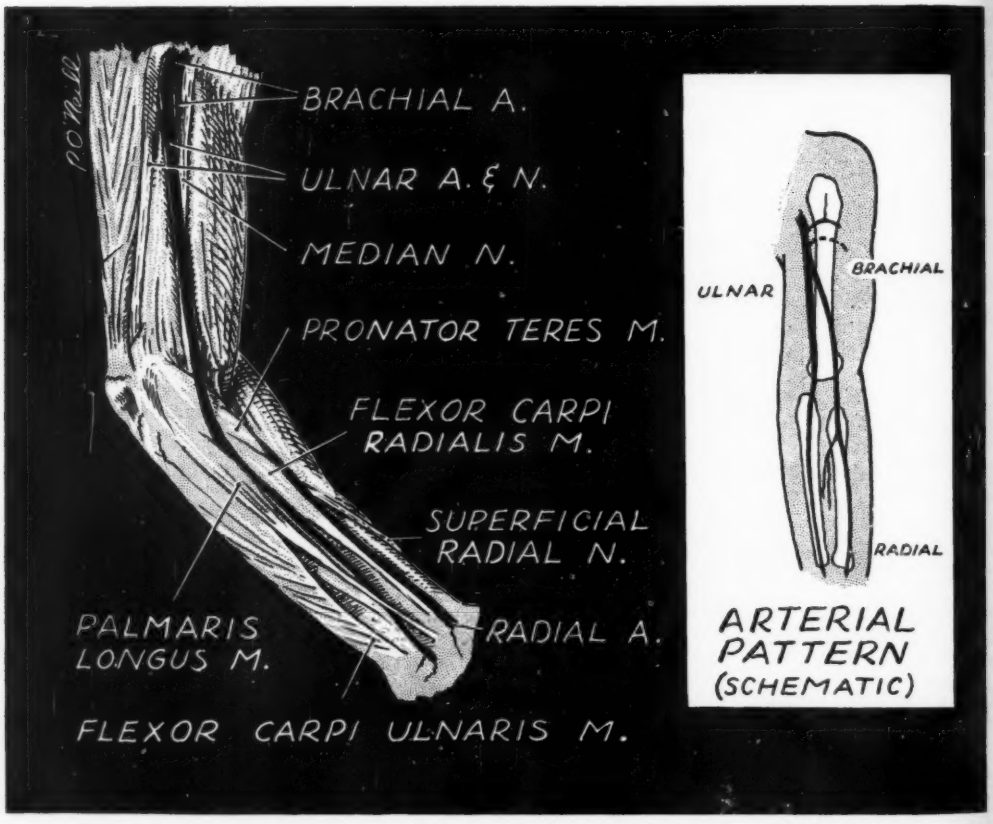
In 10 of the extremities, 2.5 per cent, the ulnar artery followed a superficial course in the forearm. Hazlitt[4] reported a superficial ulnar in 2.9 per cent of 730 extremities studied for this condition, while McCormack found it in only 1.6 per cent of 750 extremities, and Gray[3] in 1.5 per cent of 452.

The typical superficial ulnar, lying just deep to the antebrachial fascia, passed superficially from the antecubital fossa over the origins of the pronator teres, flexor carpi radialis, and palmaris longus muscles. At the middle of the forearm, it reached the lateral border of the flexor carpi ulnaris and coursed distally to attain its normal relationship just before reaching the wrist. In two specimens the artery coursed superficially as described except that it passed deep to the palmaris longus muscle near that muscle's origin.

There were three cases in which the superficial ulnar followed a very unusual course (Fig. 2). These vessels were from an extremity with an ulnar of high origin, an extremity with a superficial brachial, and one which was normal except for the superficial position of the ulnar. In each case the vessel passed superficially through the antecubital fossa and over the superficial surface of the origins of the pronator teres and flexor carpi radialis muscles. They then coursed in the groove between the flexor carpi radialis and palmaris longus, lying on the surface of the flexor digitorum sublimis. Just proximal to the wrist these vessels were in direct relation to the anterolateral surface of the median nerve where they could readily be mistaken for a persistent median artery. The vessels then curved medially to cross under the palmaris longus tendon and enter the palm in the usual manner.

The clinical importance of the superficial ulnar artery can hardly be overemphasized. Situated in close relationship with the superficial veins of the antecubital fossa, the artery may unsuspectingly be entered in attempting a venipuncture (Cohen[2]). This is especially likely since the application of a tourniquet

FIG. 2



An unusual course of a superficial ulnar artery which originated from the proximal portion of the brachial artery.

FIG. 3

Radiograph of a fetal extremity injected with a lead tetroxide mixture showing the two most common variants, a radial artery of high origin and a persistent median artery entering into the formation of the superficial volar arch.

will obliterate the pulsation of the artery.

A superficial brachial artery (Fig. 1, D) was present in 1 per cent of the current series and 1.07 per cent of McCormack's specimens. This vessel, which arose from the axillary or proximal portion of the brachial artery, lay superficial to the median nerve as it coursed down the arm, and gave origin to the radial and ulnar arteries in the antecubital fossa. The radial artery assumed a normal position, but in all four cases the ulnar artery passed superficially over the flexor muscles in one of the manners previously described.

In these specimens, the deep brachial artery was in the normal position and in three instances gave origin to the interosseous arteries of the forearm. In the fourth specimen, the brachial did not extend into the forearm, the interosseous arteries arising from the radial.

There were two examples, 0.5 per cent of accessory brachial arteries (Fig. 1, B). These vessels, both comparatively small, arose from the posteromedial side of the proximal portion of the brachial artery. They followed a course medial and slightly posterior to the brachial artery and median nerve and were closely related to the medial surface of the brachialis muscle in the distal third of the arm. They rejoined the brachial artery in the antecubital fossa at its point of bifurcation.

A persistent median artery entered into the formation of the superficial volar arch in 9 per cent of the extremities (Fig. 3). These vessels were recorded in 14 per cent of the fetal specimens and only 6 per cent of the adult. Fifteen and five-tenths per cent of the extremities from females possessed this variation, while being found in only 4.5 per cent of the male extremities. It was interesting to note that 44 per cent of the median arteries were found in extremities in which other arterial variations existed.

Summary

A study of 408 upper extremities of a heterogenous group, both male and female adults and fetuses, showed major arterial variants in 27.8 per cent. The most common variations were a high origin of the radial artery, 15.6 per cent, a persistent median artery, 9 per cent, and a superficial ulnar artery in 2.5 per cent of the extremities.

Both extremities were studied in 161 bodies, 39.4 per cent showing abnormalities in one or both arms. Among the anomalies found in this group, almost one-half of the variants occurred bilaterally. Variations were slightly more frequent in females.

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Streptococcal Enzymes in the Treatment of Pleural Empyema

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The author illustrates the use of streptococcal exotoxins in the so-called "enzymatic debridement" of instances of empyema.

REMOVAL of the pleural contents is often the crucial problem in the treatment of pleural empyema and hemothorax because re-expansion of the underlying lung and obliteration of the pleural space may follow. Conversely, failure in this direction leads to chronicity in terms of infection, pathologic changes, and physiologic effects.

There are several methods for evacuating a pleural empyema or hemothorax. Needle aspiration, the simplest and most applicable maneuver, and closed intercostal tube drainage are frequently employed with success when the pleural disease is not loculated and where the pleural contents are fluid. But these conditions frequently are not present. Instead there may be multiple loculations, thick viscid fluid, and even particulate matter which can neither be aspirated with a large caliber needle nor withdrawn with suction through a large catheter. Unfortunately, in such instances, rib resection for drainage may be contraindicated by local and systemic factors. Obviously, it is of some importance in this situation to have pleural contents which are thin, homogeneous, and uniloculated. As documented principally by Tillett, Sherry, and associates,[1-8] this may be accomplished by two products of streptococcal metabolism.

Use of Streptococcal Enzymes

Certain strains of hemolytic, pathogenic streptococci in broth cultures can produce two distinctly separate exotoxins, *streptokinase* and *streptodornase*, which may be enzymatic catalysts. Streptokinase was first described by Tillett and Garner,[9] in 1933, as a principle elaborated by hemolytic streptococci which could prevent a blood clot from forming in the presence of all the components of the clotting mechanism and, in addition, could liquify human fibrin. More recent studies by Tillett and his colleagues have categorized this factor as a proteolytic agent, which may act as a catalyst for the transformation of serum plasminogen, the inactive precursor, to plasmin, the active fibrinolytic enzyme of serum.

The role of this bacterial product in uninfected clotted hemothoraces and thick fibrinous pleural effusions with or without loculation is quite apparent. In those instances where fibrin clots prevent satisfactory aspiration by needle, the instillation of streptokinase liquifies the clots and may permit aspiration of the pleural contents. If fibrinous bands are obstacles, a multilocular pleural situation may be converted into a unilocular state by lysis of the fibrin bands.

Initial knowledge concerning streptodornase, a second principle elaborated by certain hemolytic streptococci was contributed simultaneously and independently by McCarty,[10] and Tillett and associates.[11, 12] Streptodornase can break down extracellular, nonviable macromolecular desoxy-ribose nucleoprotein to the smaller acid soluble nucleotide stage, perhaps by enzymatic digestion. The nucleoprotein element of a pleural exudate is the real impediment to aspiration, since it furnishes the exudate with its characteristic thickness and high viscosity. Following the intrapleural administration of streptodornase the thick viscous fluid becomes thin and this exudate may be aspirated.

Streptococcal enzymatic debridement is produced clinically by the application of the two enzymes simultaneously to the intrapleural material since so often fibrin and nucleoprotein are both present. Removal of the necrotic slough and cellular debris ap-

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parently helps to sterilize the pleural cavity in the presence of antimicrobial agents. In addition streptococcal debridement may progress to actual decortication if the enzymes are applied at an early stage in the formation of the cortex. This may be exemplified in case 1 described below.

To illustrate the possible chain of events which may follow the use of streptokinase and streptodornase, two patients with empyema are presented. The treatment schedule employed was arbitrary.

Case Report

Case 1. G. L. (No. 77493), a 17 year old, white man, was referred by Dr. J. G. Jantz of Bedford, Va., to the service of Dr. I. A. Bigger at the Medical College of Virginia Hospital because of a left pleural empyema.

The patient was shot in the left chest eight weeks prior to admission. The initial traumatic hemothorax was treated by closed intercostal tube underwater drainage. On admission to this hospital, there was paradoxical respiration on the affected side, prominent and approximated ribs with depressed interspaces and pronounced atrophy of the pectoral and intercostal muscles of the left side. Severe retraction of the left costal cage was present and an empyema cavity from which a coagulase positive *Staphylococcus aureus* was cultured (Fig. 1).

Initial treatment of this empyema, which was about 200 cc. in volume, consisted of systemic penicillin and Aureomycin, local penicillin, blood transfusions, underwater catheter drainage with high negative pressure, and breathing exercises. Drainage was meager and the lung did not expand. Accordingly, the patient was scheduled for surgical decortication.

On the afternoon prior to the proposed operation, it was decided to attempt enzymatic decortication. Therefore, 180,000 units of streptokinase and 60,000 units of streptodornase in 10 cc. of saline were instilled through the intercostal tube and the tube clamped for eight hours. At the end of this time 200 cc. of thin serosanguinous fluid was easily aspirated through the tube. The tube was then reconnected

FIG. 1

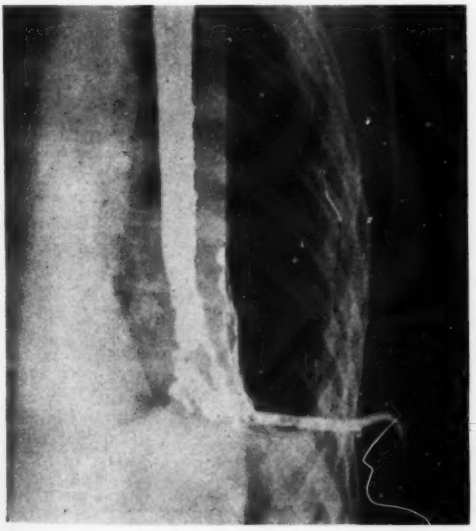


FIG. 2

FIG. 3

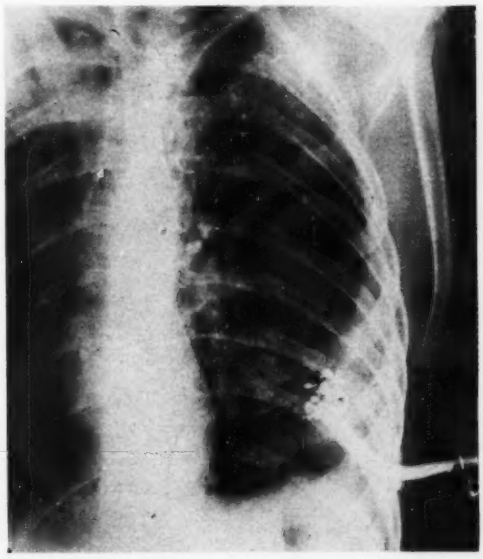


FIG. 4

to underwater drainage with suction for 16 hours, disconnected and aspirated, and the same amount of enzyme instilled. This routine was followed for 20 consecutive days. During the first few days approximately 150 cc. of fluid was obtained daily, but this gradually diminished in amount as the empyema space became smaller. The coagulase positive *Staphylococcus aureus* could no longer be isolated.

After one week of enzyme treatment, the empyema cavity was approximately half its previous size. After three weeks of enzyme treatment and intercostal tube drainage with negative pressure, the cavity volume was about 35 cc. (Fig. 2). The vital capacity had increased from 51 to 70 per cent of normal and the thoracic cage deformity and muscle atrophy on the

FIG. 5

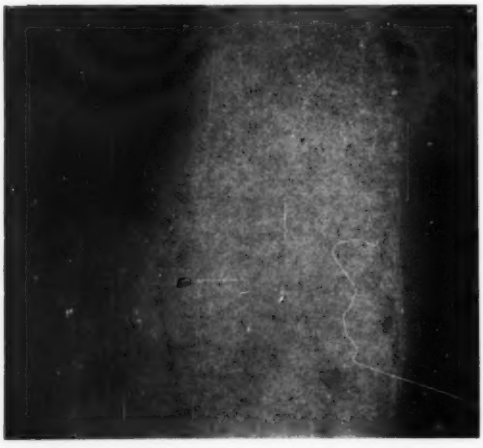


FIG. 6

affected side had become less pronounced. The patient was discharged from the hospital at this time on open intercostal tube drainage (Fig. 3). Seven weeks later the No. 22 urethral catheter was removed from a small fistula. The vital capacity was 95 per cent of the estimated normal, and the patient appeared well. Five weeks later, the sinus was healed, weight loss had been regained, the vital capacity was 105 per cent and the patient was completely rehabilitated (Fig. 4).

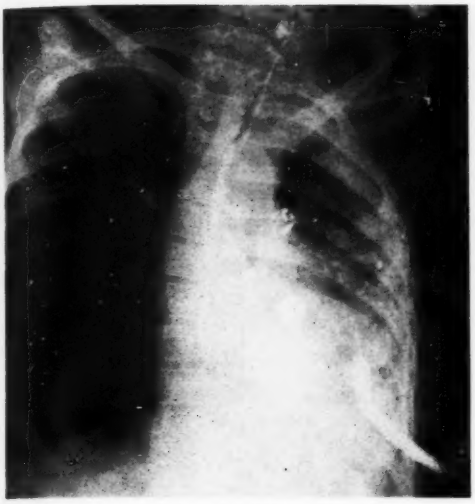
Re-expansion of the underlying lung and affected chest wall took place with the same type of underwater drainage that had failed previously. It would seem that pulmonary expansion was being accomplished by enzymatic decortication of the incarcerating cortex.

Case 2. P. N. (No. 84165), an 8 year old, white girl, was admitted to the service of Drs. Edmonds and Kendig at the Medical College of Virginia Hospital with left upper and lower lobe pneumonia and a left pleural empyema (Fig. 5).

The early hospital treatment consisted of systemic Aureomycin and penicillin, blood transfusions, and needle aspirations of the empyema followed by penicillin locally. The pleural exudate was negative for bacteria and tumor cells. Needle aspiration yielded 900 cc. of thick, fibrinous, serosanguinous fluid during the first four hospital days. It then became impossible to aspirate in spite of multiple puncture sites. Mediastinal shift, dyspnea and cyanosis developed. Intercostal tube drainage was done by Dr. I. A. Bigger and 250 cc. of sanguinous fluid was evacuated. In spite of continuous underwater drainage, no further fluid could be obtained.

Lipiodol instillation at this time showed a basilar empyema cavity with a volume of 150 cc. (Fig. 6).

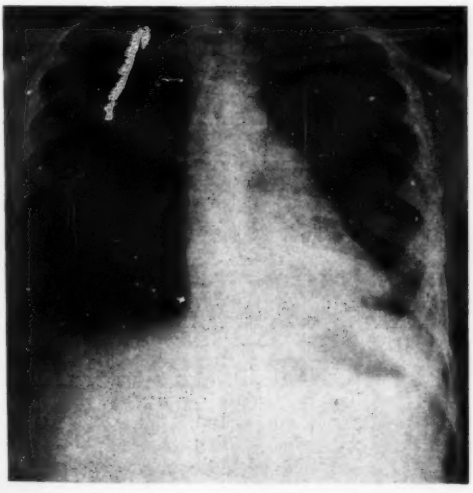
FIG. 7



The instillation did not instigate coughing, nor was a bronchopleural fistula demonstrated. Then 180,000 units of streptokinase and 60,000 units of streptodornase in 10 cc. of saline were instilled through the intercostal tube and the tube clamped for eight hours. At the end of this time 300 cc. of thin, reddish-brown fluid was aspirated through the tube. The tube was then connected to simple underwater drainage for 16 hours, disconnected, aspirated, and the same amount of enzyme instilled. This routine was followed for six consecutive days; between 30 to 100 cc. of pleural exudate was obtained daily.

On the sixth day of treatment lipiodol instillation stimulated coughing and demonstrated the presence of a bronchopleural fistula (Fig. 7). This was verified on a subsequent occasion. Enzyme therapy was stopped. Intercostal tube underwater drainage was continued and then converted to open tube drainage. The empyema cavity gradually became smaller and finally was obliterated (Fig. 8).

FIG. 8



The bronchopleural fistula may have evolved from the pneumonic process, pressure necrosis by the intercostal tube, enzymatic digestion, or a combination of these factors. However, it would seem that the use of enzymatic debridement in pulmonary trauma, either bacterial or physical, might instigate the formation of a bronchopleural fistula. Accordingly, enzymatic therapy should be used with caution if the possibility of a fistula exists and perhaps not at all if a fistula is present.

Summary

(1) Some problems of treatment in complicated hemothoraces and empyemas are presented.

(2) The place of streptokinase and streptodornase in the treatment of certain pleural diseases is discussed.

(3) Two case histories illustrate the possibilities, both favorable and unfavorable of so-called "enzymatic debridement."

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Acute Monocytic Leukemia: Report of a Case Treated With Cortisone and 6-mercaptopurine

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MONOCYTIC LEUKEMIA was originally described in 1913 by Reschad and Schilling-Torgau.[1] Since that time numerous case reports and several reviews of the subject have appeared.[2, 3, 4] Differences of opinion about the classification of these cases were numerous in the early literature. Some cases of monocytic leukemia were considered to be reticuloendothelioses, others as variants of granulocytic leukemia.[2] Different ideas about the origin of the monocyte seemed largely responsible for the variation in thinking. Belding and associates recently separated histiocytic leukemia from monocytic leukemia on the theory that the monocyte is a specific bone marrow component and does not arise from the general reticuloendothelial system.[5] Others believe, on good evidence, that the monocyte is a derivative of the reticuloendothelial system.[6, 7]

However, in general, some cases of so-called monocytic leukemia with high monocyte counts in the peripheral blood show no proliferating monocytes in the bone marrow or other reticuloendothelial tissues. Instead, the bone marrow reveals an overgrowth of young granulocytes. Such cases have been termed the Naegeli type of monocytic leukemia, and are generally regarded as a form of granulocytic leukemia.[2, 8] True monocytic leukemia, designated as the Schilling type, shows proliferating young monocytes not only in the bone marrow, but also in the lymph nodes, spleen, liver and other tissues.[8] Skin manifestations are especially frequent in monocytic leukemia, and painless, firm nodules in the skin containing collections of monoblasts have been described as specific for this type of leukemia.[9] Petechiae are also usually present.[4]

The following case of acute monocytic leukemia was treated with cortisone and 6-mercaptopurine. It was complicated by the presence of diabetes mellitus and a biologic false positive test for syphilis.

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Case Report

Chief Complaint. This 58 year old white man was admitted to the Memorial Hospital on July 27, 1954, complaining of arthritis.

Past History. The patient had "rheumatism" 12 years before which was relieved by extraction of his teeth, in 1942. On November 29, 1950, a Kahn test was negative and a chest x-ray within normal limits. The urine was essentially negative, the hemogram normal. One year before admission, a V. D. R. L. slide test was weakly positive, a Kolmer test doubtful. The hemogram and urine were again within normal limits.

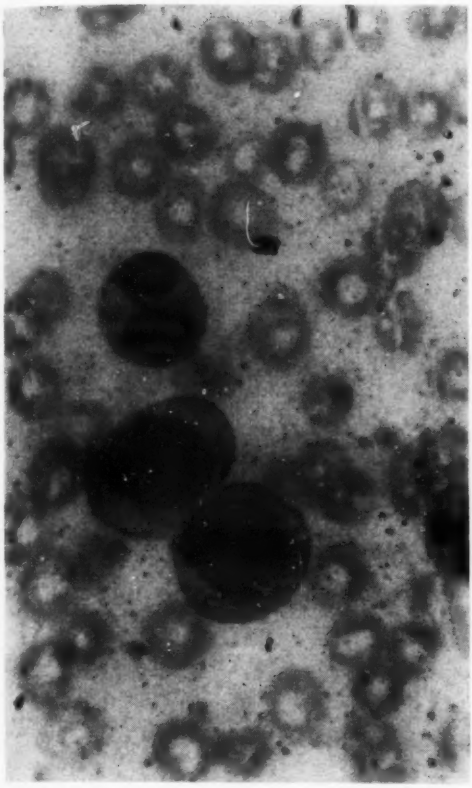
Family History. His mother died at 73 with cancer of the stomach. One sister died of diabetes. The father died of old age; two brothers and one sister died of heart trouble.

Present Illness. During the month before admission, the patient had a poor appetite accompanied by weight loss, and he tired easily. For two weeks before admission, there was a migratory aching in his right arm, radiating to his right shoulder. Two days before admission the patient developed an aching pain in the left leg associated with pain in the left groin. Also, a crusted lesion of the lower lip was noticed about this time.

Physical Examination. The skin was warm and dry. Blood pressure was 140/80, T. 98.6°, P. 100, R. 20. He wore dentures; a crusted lesion was present on lower lip. The thyroid gland was nodular; cervical lymph nodes were enlarged. Heart and lungs were not remarkable. Spleen and liver were palpable and moderately enlarged. The inguinal and axillary lymph nodes were moderately enlarged, nontender. There was some pain in the lower back and left knee on motion.

Special Examinations. On admission, Hgb. was 9.4 Gm., RBC 3,150,000, WBC 35,250 with 14 bands, 13 seg., 7 lymph., 3 mono., 14 metamyelocytes, 3 myelocytes, 46 monoblasts, 2 normoblasts per 100 WBC. The smear was characteristic of monocytic leukemia (Fig. 1). Sedimentation rate was 120 mm. per hr. (Westergren). The V. D. R. L. test was positive. Urine was yellow, clear, acid, with a specific gravity of 1.022, albumin negative, sugar 4+, acetone negative; microscopic examination showed 1-2 WBC and an occasional hyaline cast. On July 29, a second

FIG. 1



Peripheral blood smear showing two monoblasts and one monocyte. Note the rather abundant cytoplasm.

V. D. R. L. test was positive. WBC were 35,300 with 51 monoblasts, 10 bands, 19 seg., 12 lymph., 4 mono., 1 myelocyte, 3 metamyelocytes and 3 normoblasts per 100 WBC. A blood sugar was 440 mg. per 100 cc. The urine sugar again 4+, and now 10 mg. of albumin per 100 cc.

Chest x-ray film showed the heart to be normal in size and contour. The diaphragm was smooth, the costophrenic angles clear. The lung fields and retrocardiac space were also fairly clear. There was moderate hypertrophic arthritis of the dorsal spine.

On August 3, Hgb. was 9.1 Gm., RBC 3,390,000, WBC 62,400 with 4 bands, 7 seg., 11 lymph., 4 mono., 20 metamyelocytes, 3 myelocytes, 51 monoblasts and 20 normoblasts per 100 WBC. On August 9, urea nitrogen was 22 mg. per 100 cc., Hgb. 9.1 Gm., RBC 3,390,000, WBC 28,400, 22 bands, 12 seg., 16 lymph., 5 mono., 10 metamyelocytes, 5 myelocytes, 30 monoblasts, 14 normoblasts per 100 WBC.

Course in Hospital. On July 28, cortisone, 100 mg., 4 times daily, was begun. On the next day it was dropped to 75 mg., 4 times daily. The temperature rose to 102° F. on that day, but returned to normal by July 31. The diabetes was regulated with 40 units of NPH insulin daily and an 1800 calorie diet. On August 1, the cortisone was reduced to 50 mg., 4 times daily. Five hundred cc. of whole blood were given on August 4 and 5. August 6, 6-mercaptopurine, 50 mg., 3 times daily, was started. The patient improved symptomatically and was discharged on August 12, 1954, to continue cortisone, insulin and 6-mercaptopurine.

Subsequent Course. Headaches and mental confusion developed on August 15. Small petechiae appeared over the abdomen. He became progressively more confused.

He was readmitted to the hospital on August 18. He was irrational. Blood pressure was 118/80, T. 99.2°, P. 100, R. 22. There were numerous petechiae, old and new, over the abdomen. Several white, nontender nodules 5 mm. in size, were noted on the scalp. The axillary, cervical and inguinal nodes were still enlarged, nontender and firm. The liver was down three finger-breadths, but the spleen was not felt.

Antileukemic therapy was discontinued. On August 18, the patient was given 500 cc. of whole blood. On August 20, the Hgb. was 7.2 Gm., RBC 2,790,000, WBC 6,250, with 15 bands, 12 seg., 43 lymph., 5 mono., 2 metamyelocytes, 2 myelocytes, 1 eos., 1 baso., 17 monoblasts and 22 normoblasts per 100 WBC. On August 24, a third pint of blood was given. By August 27, leukemia cutis was evident over the abdomen in the form of white small deep-seated nodules about 0.5 cm. in diameter like those on the scalp. On August 28, the Hgb. was 8.1 Gm., RBC 2,790,000, WBC 12,000, 15 bands, 12 seg., 21 lymph., 1 eos., 6 baso., 15 metamyelocytes, 5 mono., 7 myelocytes, 17 monoblasts, 7 normoblasts per 100 WBC.

6-mercaptopurine 50 mg. daily was again begun on August 29. By the next day the sensorium had cleared somewhat and three days later the patient was mentally clear. At this time the Hgb. was 7.4 Gm., RBC 2,670,000, WBC 13,800, with 16 bands, 10 seg., 16 lymph., 8 mono., 15 metamyelocytes, 1 myelocyte, 31 monoblasts, 3 baso. He was discharged on September 3.

The patient was readmitted on September 29, 1954, because of severe weakness. He had developed generalized edema and scattered subcutaneous hemorrhages. Blood pressure was 98/60, T. 98.4°, P. 130, R. 26. Spleen and liver were enlarged; axillary, inguinal and cervical lymph nodes were enlarged. There was dullness over both lung bases. 6-mercaptopurine was increased to 50 mg., 3 times daily. One pint of blood was given. The Hgb. was 7.6 Gm., RBC 2,670,000, WBC 94,000, with 2 bands, 12 lymph., 1 myelocyte, 85 monoblasts.

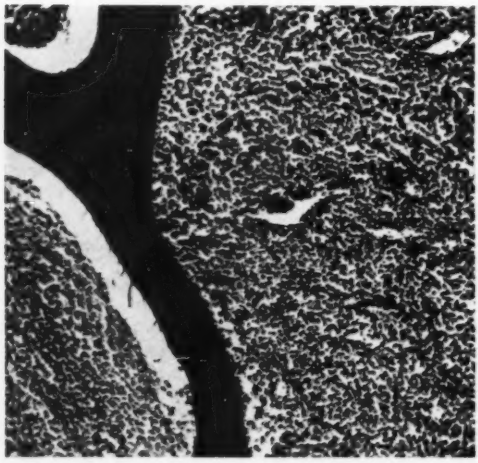
The patient died on October 1, 1954. *Final clinical diagnoses* were: acute monocytic leukemia; diabetes mellitus.

Autopsy Findings. The body showed petechiae over the abdomen, legs and arms, edema of the ankles, and easily palpable, enlarged cervical, axillary and inguinal lymph nodes. Deeply seated in the skin over the forehead, scalp, face, abdomen and chest were firm, whitish nodules averaging 5 mm. in diameter, more easily palpable than seen. The gums were pale, the mouth edentate.

On internal examination, petechiae were seen over the serosal surface of several loops of the bowel and the stomach.

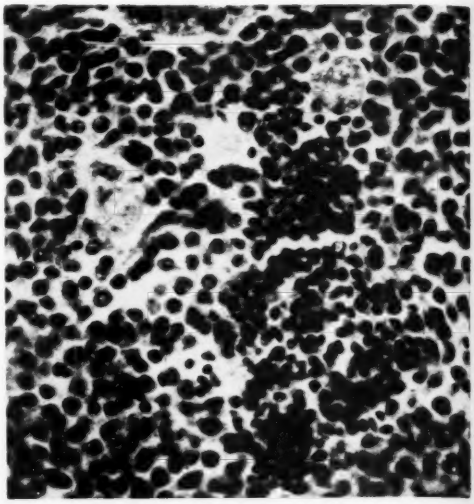
Gross Examination. The heart weighed 400 Gm., had a smooth epicardium with numerous petechiae over the surface, especially near the base. The myocardium was pale and flabby. The endocardium was glistening, smooth and the valves were within normal limits. There were a few atheromatous plaques within the coronary vessels, but no evidence of occlusion. The lungs weighed 720 and 790 Gm., being extremely wet and boggy. Their surfaces were dark reddish-brown; a large infarct was present in the right lower lobe 8 cm. in diameter, the pulmonary vessel supplying this area containing an organized embolus. The bronchial lymph nodes were moderately enlarged up to 2 cm. in diameter. The cervical, axillary, inguinal, abdominal and thoracic lymph nodes all showed moderate enlargement, some up to 3 cm. in diameter with replacement of the normal lymph node tissue by a pale, grayish-green, soft, spongy tissue. The spleen weighed 800 Gm. and was firm. It had a mottled, reddish-brown cut surface, more pale than usual; light tan flecks were scattered over this surface. The right kidney weighed 230 and the left 210 Gm. Both were pale, mottled grayish-tan and on section showed diffuse streaking with pale tan tissue in the cortex and along the collecting tubules; the pelves and papillae contained extensive petechiae. The liver weighed 2350 Gm. and had a slightly granular surface with an intact capsule. The pale brown parenchyma showed focal whitish flecks throughout, sometimes more marked in the portal areas. The adrenal glands together weighed 25 Gm. and appeared to be moderately enlarged. They had a greenish-gray appearance in the medullary region. The bone marrow had a pale brown mushy appearance. It appeared similar in the vertebrae, sternum and ribs. There were petechiae in the bladder and over the serosa of the bowel. The pancreas and thyroid gland were grossly unremarkable. Examination of the brain was restricted.

FIG. 2



Bone marrow section (X110) showing complete replacement of marrow by monocytic cells.

FIG. 3



Section of lymph node (X 510) demonstrating a few remaining lymphocytes (small dark cells near center) almost completely overrun by large monocytic cells with fairly abundant cytoplasm.

Microscopic Examination. Nearly all of the organs and tissues were involved by cells of monocytic leukemia. The bone marrow showed extensive replacement of the normal myeloid tissue by a homogeneous sheet of large monoblasts packed closely together between trabeculae, excluding all fat and other marrow elements (Fig. 2). Foci of hemorrhage and necrosis were scattered about. Individual cells were large, contained a moderate amount of pinkish staining cytoplasm on H and E preparations, and a large vesicular nucleus which was indented, lobed or round, with sometimes prominent chromatin granules. The cells in some areas appeared to be arranged in a cord-like fashion as if in a reticulum network. Lymph nodes were extensively overrun by monocytic leukemia cells replacing the normal nodal architecture. Only a few scattered nests of lymphocytes remained which stood out in contrast to the larger cells of monocytic leukemia (Fig. 3). Some of the nodes appeared similar to reticulum cell sarcoma. However, reticulum stains showed no increase in reticulum in the nodes or skin. Mitotic figures were prominent throughout the sheets of proliferating leukemia cells. The spleen likewise showed extensive infiltration and replacement of its normal architecture by the cells of monocytic leukemia. These cells lined the sinusoids and involved the white pulp. The involvement here was diffuse, more or less following the normal architecture of the spleen and enlarging upon it, but not actually forming any tumor masses. In the liver, monoblasts were seen in the sinusoids and periportal spaces in great collections but nowhere forming prominent tumor masses. Infiltration was also seen in the kidney with monoblasts in the renal fat, the pelves, along the collecting tubules and among

FIG. 4

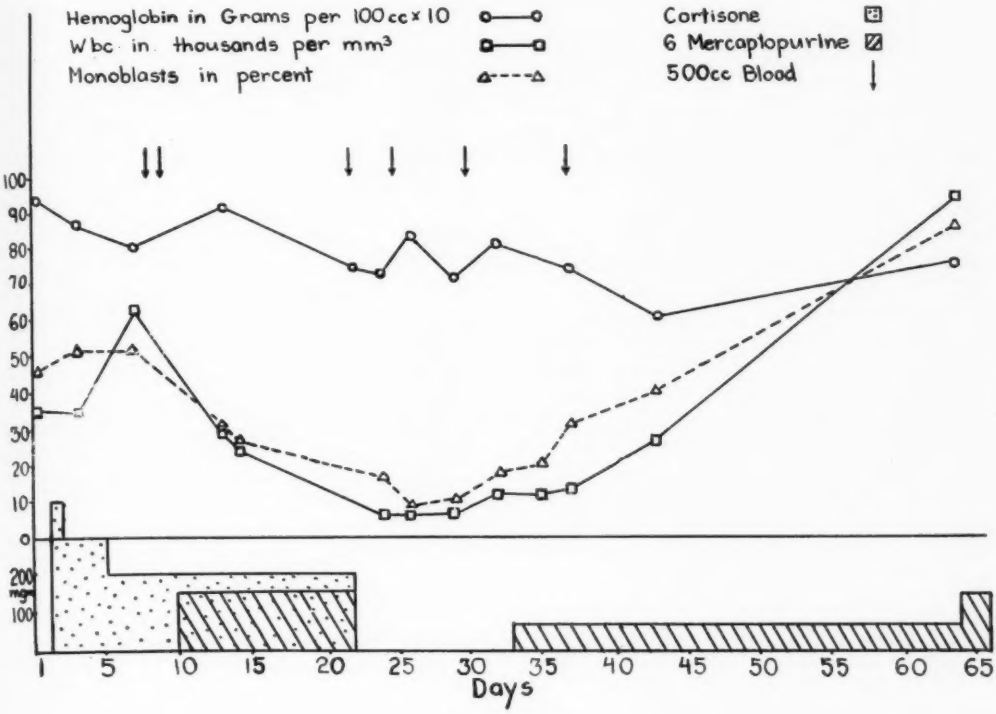


CHART I

the glomeruli in the cortex. The cells were the same everywhere, large monoblasts and monocytes. There was extensive involvement of the adrenals, large bowel, epicardium, myocardium and thyroid with monoblasts and monocytes. The pancreas was infiltrated moderately with monocytic cells, especially around the periphery. A few monocytes were seen in the islets of Langerhans, but these did not appear numerous enough to affect the islet cells. No hyaline changes or other microscopic lesions associated with diabetes mellitus were found.

The skin presented a typical picture of monocytic leukemia with collections of monoblasts in the dermis around the hair follicles and glandular structures as well as in the margins of the subcutaneous fat. The lungs showed emphysema, focal collections of monoblasts and a pulmonary embolus in the right lung with a partly organized pulmonary infarct.

The *diagnosis at autopsy* was acute monocytic leukemia (Schilling type), with involvement of many organs and tissues.

Comment

This case of acute monocytic leukemia presented with symptoms of arthritis, a fairly frequent initial complaint.[3, 4] The peripheral blood smear revealed a rather large percentage of monoblasts. Other characteristic features included deep-seated skin nodules, the replacement of bone marrow and lymph node architecture by sheets of monocytes and monoblasts sometimes associated with reticulum fibers.[3, 6]

This patient was treated with cortisone and 6-mercaptopurine. There was a marked drop in white count (Chart I) and a reduction in the percentage of monoblasts. Transient symptomatic improvement also occurred. However, the disease continued its unremitting course despite treatment. In retrospect (Chart I), it appears that an increase in the dose of 6-mercaptopurine during the second month of treatment might have prevented the gradual rise in white count during that period. Whether such a change in treatment would have increased the survival time is questionable. It should be mentioned that the prominent skin nodules, petechiae and cerebral symptoms developed while the patient was being given 150 mg. 6-mercaptopurine daily

along with 200 mg. of cortisone. Burchenal and associates carried one of their cases of monocytic leukemia at least three months on 6-mercaptopurine after she had failed to respond to cortisone.[10] There was a decrease in white count, maintenance of hemoglobin, return of marrow findings toward normal, disappearance of mouth ulcers, and an increase in strength. The dose they employed was 175 mg. per day given more or less regularly. However, two of their three cases receiving adequate trial with 6-mercaptopurine failed to show a favorable response.[10]

An unusual feature of our case was the presence of a biologic false positive test for syphilis. A V. D. R. L. slide test was positive two times during the disease. No other indication of syphilis was obtained clinically, and at autopsy no evidence of syphilis was found in the tissues. Evans states that the various laboratory tests for syphilis have been consistently negative in monocytic leukemia.[4] As far as we are aware, no other case of monocytic leukemia has been reported showing a biologic false positive test for syphilis.

It is interesting that diabetes mellitus also became manifest at the time of the onset of the leukemia. Microscopically, there was some infiltration of the pancreas and islets of Langerhans by monocytic cells, but apparently not enough to affect their function. Perhaps the stress imposed by the leukemia provoked the diabetes to become manifest at that time. However, we can only regard the diabetes as incidental, as there was a history of diabetes in one sister.

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Defects of the Cardiac Septa: Diagnosis and Surgical Treatment*

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The closure of septal defects offers a challenge to the surgeon. Since the closure of such defects is now feasible, the correct diagnosis should be established preoperatively.

DEFECTS OF THE INTERATRIAL and interventricular septa are perhaps the commonest of all congenital malformations of the heart. Until recently, a general diagnosis of "septal defect" was considered to be adequate in such patients because in many instances the clinical course was thought to be relatively benign and particularly because there were no available methods of surgical correction. As more interest is being focused on the surgical treatment of congenital cardiac anomalies, the pathophysiologic disturbances caused by septal defects have assumed greater significance, and a complacent attitude toward these lesions is no longer acceptable. Accurate diagnosis is essential in virtually all such cases because in many instances surgical repair may now be accomplished. In general the degree of disability depends upon the size of the defect and the volume of the intracardiac shunt. Because of the striking similarity which may exist between cases of auricular and ventricular septal defects as well as other defects causing left to right shunts, the final diagnosis usually rests with cardiac catheterization, although other diagnostic methods including angiocardiography are still important. In an occasional case where the findings may be puzzling or equivocal, final diagnosis may be settled by surgical exploration. Some of the more significant features of congenital defects of the cardiac septa will be presented here including the findings of cardiac catheterization, and recent developments in surgical treatment will be considered.

*Supported in part by grants from the Houston District Chapter, Texas Heart Association, and the Cora and Webb Mading Fund for Surgical Research, and the Junior League of Houston Memorial Fund.

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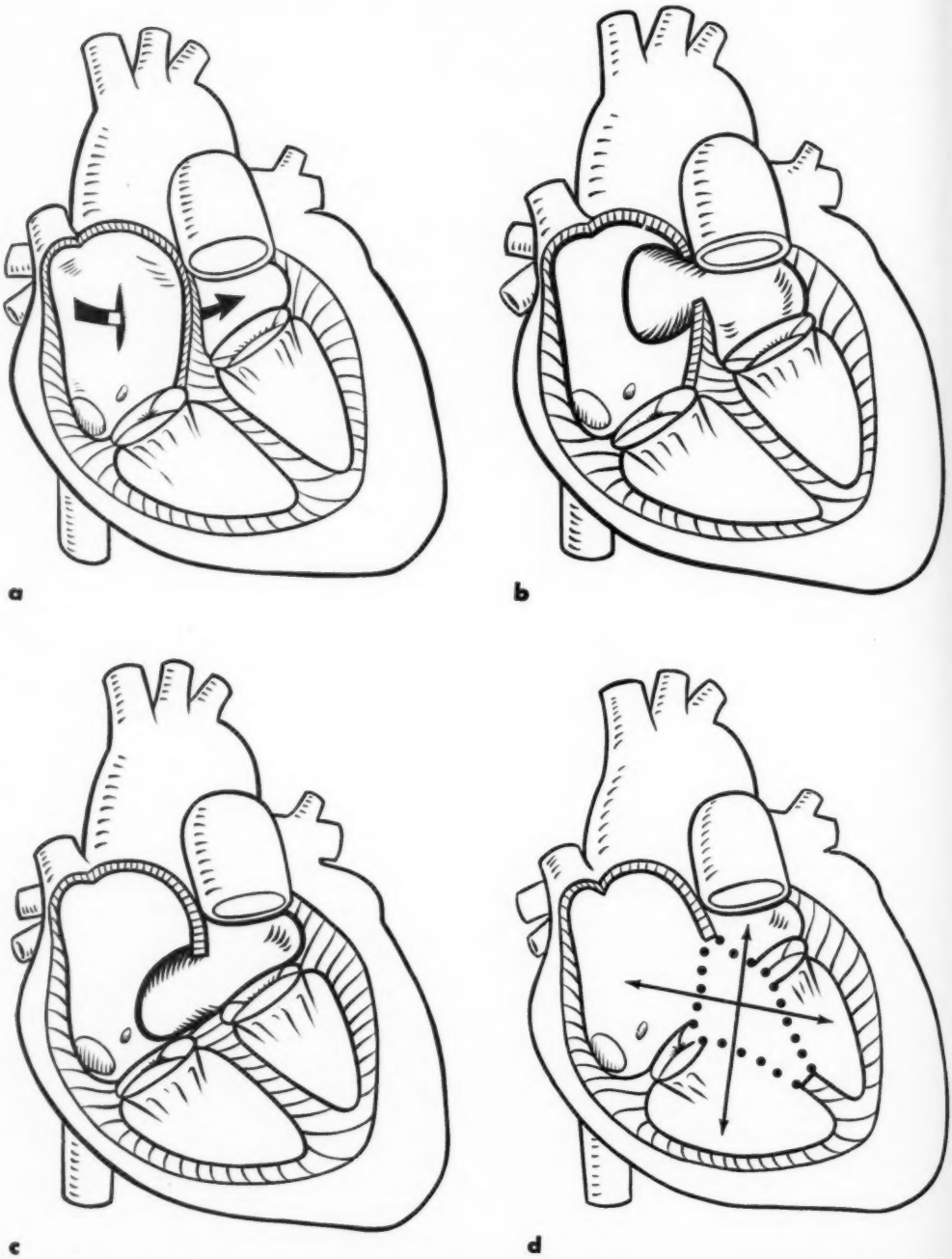
Atrial Septal Defects

During fetal life defects of the interatrial septum cause no disturbance; the blood is directed from right to left in the normal manner. After birth, however, when left atrial pressure exceeds the pressure in the right, the flow reverses. A left to right shunt produces a pulmonary flow greater than systemic and consequently an increased burden on the right ventricle.

Defects of the atrial septum of clinical significance represent true failures in the embryologic development of the interatrial partition. A persistently patent foramen ovale usually being small and slit-like and having a valvular arrangement causes no appreciable cardiac disturbance inasmuch as it tends to remain functionally closed during the cardiac cycle (Fig. 1-a). Only under conditions in which right atrial pressure is elevated does the flap remain open and permit an intracardiac shunt. The commonest true defect of the atrial septum is the ostium secundum which occupies the mid portion of the septum and is surrounded by a rim of septal tissue (Fig. 1-b). The septum primum defect lies in the lower portion of the atrial septum, the inferior border being the mitral and tricuspid valves (Fig. 1-c). A third type of defect is known as the atrioventricularis communis, which is an ostium primum defect plus a large high ventricular septal defect (Fig. 1-d). The mitral and tricuspid valves are then joined together so that one valve ring is present. In general those defects of the inferior margin of the atrial septum cause the greatest disturbance of cardiac function.

Under ordinary circumstances, there is no cyanosis. Mottling of the skin is not infrequently present and may be confused with true

FIG. 1



Drawings of the heart showing the various types of interatrial septal communications which may produce left-to-right intracardiac vascular shunts. The slit-like opening of a patent foramen ovale is shown in (a). Other drawings illustrate true interatrial septal defects of the (b) ostium secundum, (c) ostium primum, and (d) atrioventricularis communis types.

cyanosis, but is differentiated by the normal color of lips and nail beds. The gracile habitus, supposedly characteristic of patients with atrial defects, is by no means constant, and the patient with a large incapacitating defect may have a normal growth pattern.

Frequently the thorax over the precordium is deformed. The prominence being due to a dilated right ventricle. The systolic murmur in these cases is probably produced in the dilated pulmonary artery and not by the defect itself.[13]

At birth a murmur is usually absent, and even when it becomes audible there may be considerable variation in its location and intensity. Characteristically it is soft, blowing and maximal in the left second or third intercostal space. The pulmonary second sound is accentuated, and in the frequent presence of right bundle branch block the sound is widely split.

Roentgenographically cardiac enlargement, principally right ventricular, is evident, with prominence of the pulmonary conus and pulmonary vascular shadows. In large defects fluoroscopy may reveal the so-called "hilar dance."[13] Electrocardiography indicates right ventricular hypertrophy and often right bundle branch block. In the absence of such findings, a presumptive diagnosis of atrial septal defect should not be made.

Cardiac catheterization reveals the presence of oxygenated blood in the right atrium, although occasionally the presence of anomalous pulmonary veins into the right atrium may lead to some difficulty in diagnosis. In infants and children the pulmonary arterial pressure is often normal in the ostium secumdum defect, but in the adult the pressure increases and may subsequently equal systemic arterial pressure (Table 1).

With increasing age right ventricular hypertrophy advances and many patients develop severe pulmonary hypertension. Although this defect may be compatible with a relatively normal infancy and childhood, frequently during early adulthood incapacitating symptoms appear. Thus, cases must be selected for surgery at an early age when the cardiac reserve is greater and risk of operation low.

Ventricular Septal Defects

The degree of cardiac disturbance produced by isolated defects of the interventricular septum depends upon the size and location of the opening. In the *maladie de Roger* where the defect is relatively small and located in the muscular portion of the septum, a rel-

TABLE 1

DATA ON PATIENTS OPERATED UPON FOR CLOSURE OF CARDIAC SEPTAL DEFECTS

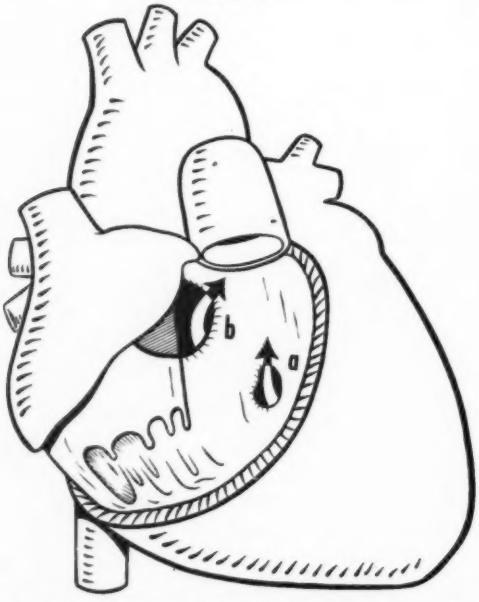
Case		*Catheterization*				*Operation*	*Type of Defect*
Atrial Defects		*Superior Vena Cava*	*Right Auricle*	*Right Ventricle*	*Pulmonary Artery*		
1. J.B. 6 M C	O_2 content (vol. %)	6.1	13.4	14	13.3	3-22-54	Ostium primum 2.5 cm.
	Pressure (mm. Hg.)		13/7	88/0	75/35		Ostium secundum 2.0 cm.
2. M.S. 25 F W	O_2 content (vol. %)	11.7	16.0	16.3	15.7	6-11-54	Ostium primum 4.0 cm.
	Pressure (mm. Hg.)	5.0	5.0		83/40		Ostium secundum 1.5 cm. Mitral stenosis
3. M.P. 31 F W	O_2 content (vol. %)	13.8	17.2	16.3	16.0	8-3-54	Ostium secundum 4.0 cm.
	Pressure (mm. Hg.)		3.0	38/5	30/8		
4. G.B. 12 M W	O_2 content (vol. %)	13.4	16.1	15.8		12-4-54	Ostium primum 4.0 cm.
	Pressure (mm. Hg.)			40/0			
Ventricular Defects							
5. A.L. 1½ M W	O_2 content (vol. %)	7.1	7.7	11.2	11.7	11-22-54	Membranous septum
	Pressure (mm. Hg.)			65/0	58/12		
6. C.J. 9 F W	O_2 content (vol. %)	9.7	9.7	13.9	13.6	12-31-54	Membranous septum
	Pressure (mm. Hg.)		42/0	35/10	38/12		

atively harsh murmur is present, but the effects upon cardiac function may be mild and most patients are asymptomatic (Fig. 2-a). If the lesion is in a "high" position in the membranous portion of the septum as is true of more than 80 per cent of cases, and if the defect is of considerable size, the anomaly may be of greater clinical significance (Fig. 2-b). Progressive cardiac enlargement is an early warning sign in the asymptomatic patient that cardiac failure is impending. Cyanosis in isolated ventricular defects is absent; but if pulmonary hypertension develops as in Eisenmerger's complex, cyanosis may subsequently appear as a right to left shunt develops.

The murmur of ventricular defects may vary from the harsh murmur of *maladie de Roger* to none at all. It is located in the left third or fourth intercostal space and is frequently associated with an easily palpable thrill. The pulmonary second sound is accentuated depending upon the pulmonary arterial pressure. The pulse pressure is usually widened, especially in infants, before pulmonary hypertension develops.

Roentgenograms show left ventricular hypertrophy, a prominent pulmonary conus, increased vascular markings, and frequently left atrial enlargement. Since a large patent ductus arteriosus differentiation must be made by retrograde aortography where the presence of contrast media in the pulmonary arteries confirms the presence of a ductus. The electrocardiogram shows left ventricular hypertrophy. If pulmonary hypertension develops, then right ventricular hypertrophy may occur. In these cases, mild cyanosis appears, and a faint systolic murmur may be present, accompanied by a high-pitched diastolic murmur of pulmonary insufficiency.

FIG. 2



Drawing of the heart showing the interventricular septum demonstrating in (a) the small defect of *maladie de Roger* and in (b) the larger defect of the membranous septum which produces more significant cardiac disability.

Cardiac catheterization reveals oxygenated blood in the right ventricle and unmixed venous blood in the right atrium; the pressure in the right ventricle and pulmonary artery may or may not be elevated (Table 1). Differentiation of the high defect from a large patent ductus by catheterization may be difficult, particularly in very small patients.

Defects of the ventricular septum may lead to death from congestive failure. Although the immediate risk to life may not be great, in many patients a high morbidity rate prevents normal growth and development. As surgical treatment of ventricular defects is perfected and improved, the clinician will be further challenged in the selection of patients for operative correction.

Surgical Treatment

Until relatively recently no satisfactory methods were available for surgical correction of defects of the cardiac septa, but during the past few years such lesions are being treated successfully with acceptable risk. In general the technics of closure of such defects include (1) the open and (2) the closed methods. According to some investigators exposure of the cardiac septa is essential for effective closure of septal defects. Gibbon and his associates[10] have pioneered in the development of an artificial heart-lung machine for open heart surgery during total interruption of the circulation, but the clinical application of this method has been very limited. Induced general body hypothermia is another method which has been advocated by Bigelow and his associates[2] and used clinically by Lewis[8] and Swan[11] for closure of septal defects under direct vision. By artificially lowering the patient's body temperature from 98.6° F. to a

hypothermic level of approximately 85° F., metabolism of the tissues of the central nervous system is reduced. Thus, cessation of arterial supply to the brain and spinal cord may be tolerated for periods up to 15 or 20 minutes without producing significant damage to the central nervous system. Interruption of cardiac inflow by occlusion of the vena cava under these circumstances permits open cardiac surgery in a dry field. Although technics of open cardiac surgery offer obvious advantages over the closed methods for closure of septal defects, the need for complicated mechanical apparatus, the threat of air embolism, and the frequent occurrence of serious cardiac arrhythmias limit their usefulness.

In the surgical treatment of defects of the atrial septum, Gross and his associates[7] have employed an "atrial well" sutured to the side of the atrium in order that sutures may be inserted into the septum in the depths of a pool of blood. By this ingenius semi-open method a number of patients have been successfully operated upon for atrial defects, but the disadvantages of operating under these circumstances are obvious and the method appears to be impractical for general use.

Closed methods of closure of septal defects are now available for successful correction of atrial and perhaps ventricular lesions, and preliminary clinical results provide reassuring evidence of the relative safety of such technics. Final accomplishment of the surgical objective has come about through an accurate understanding of certain important anatomic features of the problem, including the size and position of the defects themselves and the relationships between the cardiac septa and great vessels of the heart, coronary arteries, and conduction system.

Atrial Septal Defects. In the presence of an atrial septal defect there is usually moderate atrial enlargement. Under these circumstances the wall may be indented and sutured to the septum around the defect. Bailey and his associates[1] have developed a number of variations on a technic which they call atrioseptopexy in which the lateral wall of the septum is used to plug the defect by accurate placement of multiple sutures around the periphery of septal defects, utilizing intracardiac palpation. Although the results of such operations have been promising, the extreme deformity produced in the atrium in some instances is a definite disadvantage of the technic.

Another closed method of correcting atrial defects described recently by Björk and Crafoord[3] is the most satisfactory of all in our opinion, producing the least deformity of the atria and providing a single method for closing all types of defects. In this technic the interior of the right atrium is palpated digitally through the right auricular appendage and a suture is passed in the plane of the septum along the lower edge of the defect. As the suture is tied down outside the heart, the septum is closed completely, avoiding the openings of the vena cava, ostium of the coronary sinus, and pulmonary veins. We have modified the technic to include additional reinforcing mattress sutures which insure the permanence of the surgical closure.[5] In small lateral septal defects, however, a simple atrioseptopexy may still be the preferable method of closure.

Frequently atrial defects may be associated with anomalous drainage of the pulmonary veins. Bailey[1] reports seven such cases among 46 atrial defects treated surgically employing various corrective procedures, including transplantation of the veins to the left atrium. In exploring for an atrial defect in a 31 year old patient, we encountered an anomaly of the pulmonary veins in which the entire left pulmonary venous drainage was into the left innominate vein producing a severe left to right vascular shunt.[6] The anomaly was corrected by transplantation of the vein into the left auricle, and the patient made a complete recovery.

Ventricular Septal Defects. During the past two years a number of attempts have been made to develop a satisfactory method of closure of ventricular septal defects. At present one of the few methods of practical importance is that of Lillehei and associates[9] in which the patient is temporarily cross circulated with the parent. During total occlusion of the cardiac inflow of the patient, closure of the defect is accomplished under direct vision. Lillehei has used this procedure in 21 patients with seven deaths. Many of the patients were extremely poor surgical risks, accounting for the high mortality in this initial series.

Using experimental animals we developed a closed technic of repair inserting mattress

sutures through the upper ventricular septum avoiding interference with the outflow tracts and the major coronary vessels.[4] Although it has been used on a limited scale, this method of closure of ventricular defects which has been reported in detail elsewhere may be a useful method of surgical treatment particularly in infants and small children.

Results

Our clinical experience with surgical closure of isolated defects of the cardiac septa includes four cases with atrial and two with ventricular defects, and there have been no deaths (Table 1). Postoperative cardiac catheterization has been done in only one of these, but samples of blood drawn at operation before and after closure of the defect provide good evidence that the openings have been effectively closed. In case 3, catheterization done eight months after operation revealed that the defect was closed and the patient remains well. In fact it is our opinion based upon the satisfactory clinical course of these patients that all of the atrial defects in this series have been successfully closed. Incomplete closure of the two ventricular defects may have been obtained as evidenced by the persistence after operation of systolic murmurs of low intensity, but unquestionably the defects are greatly reduced in size and the small residual left to right vascular shunts may prove to be of no physiologic significance.

Summary

Defects of the interatrial and interventricular septa are more serious in infancy and childhood than previously appreciated.

The close clinical similarity of these two types of left to right vascular shunt usually requires cardiac catheterization for accurate diagnosis.

Recent developments in the surgical treatment of defects of the cardiac septa provide the first satisfactory means of repairing such anomalies. Four patients are reported with interatrial anomalies and two with interventricular defects in which surgical correction of the lesion has produced good results.

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The Regional Proctologic Society*

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THE LIFE of the proctologist would be considerably happier if people would quit asking him that hilarious question about 'how come' he happened to get into such a peculiar field. My answer is borrowed from our friend Orville Gass of Chattanooga, who cuts down these comedians by explaining that he got into proctology because he became allergic to halitosis. Now, if I were truthful, I might explain that in my student days we had no department of proctology but that anorectal disorders were handled by the general surgical services, as I believe, is still customary in most medical schools and teaching hospitals. Our instructors were competent teachers of surgery but, unfortunately, appeared to have a reluctant interest in proctology. Consequently, my colleagues and I learned far too little about proctology. Even as students we were aware that a considerable number of patients suffered from anorectal disorders and had an acute need of sympathy, understanding, and care which they sometimes did not receive in adequate quantities. Actually, it was this paradoxical situation which caused me to become interested in this phase of medicine. I wonder how many practicing physicians had an experience in proctology as students similar to my own?

If the foregoing sample of the lack of interest shown by some surgeons in the anorectum had been universal the picture would appear dismal, indeed. However, let us go back to the turn of the century when proctology was first established as a specialty as a result of the courage and foresight of a small group of physicians. Prior to that time the treatment of anorectal disorders was done almost entirely by irregular physicians and charlatans because of indifference on the part of the medical profession. Since then the position of proctology has steadily improved. But the ultimate goal of good care for all persons suffering from anorectal ailments has by no means been reached. This can be achieved only when the charlatan and the irregular practitioner has been eliminated and all proctology is practiced on a high level. How can we who are interested help to bring this about? An important step in this direction is to improve the type of work done by the occasional proctologist. This, I believe, is one of the most important roles of the regional proctologic society.

Only within the past couple of years has the American Proctologic Society itself become fully aware of the importance of the regional society and has appointed a special committee to investigate this field. At the present time there are 17 regional societies in this country which is not adequate. In the Southern States we now have six, not including the proctologic section of the Southern Medical Association. They are, the Southeastern, Texas, Florida, St. Louis, Mid-Western and the Piedmont societies, which, in general, serve the areas designated by their names. Compared to other sections of the country, the South has more than held its own. However, it would appear that several additional regional societies in this territory would insure every physician the opportunity to attend at least one of these meetings yearly without unwarranted inroads on his time and convenience.

The regional society with which I am most familiar is the Piedmont. The name is a bit misleading as it includes the entire states of North Carolina, South Carolina, Virginia, Georgia and Tennessee. Undoubtedly, several societies could better serve this large area. Generally speaking, I believe that this group fulfills the purpose of the regional proctologic society admirably. For this reason, I would like to describe briefly how it functions. One-day meetings are held twice yearly in various cities in the area. The local resident acts as host and is in charge of the program. All qualified physicians who have any interest in proctology are welcomed. The papers are short, practical and of such nature as to promote free discussion. The occasional proctologist is made to feel that he is an

*Chairman's Address, Section on Proctology, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

important member of the group as, indeed, he is. All are encouraged to take an active part in discussion by the completely informal nature of the meetings. The experience of the seasoned well-trained members, for which there is no substitute, is always available. Whenever possible operative clinics are held. To the occasional proctologist these are invaluable. Here he may observe at first hand, and often for the first time, proper anorectal operative technics. Even the experienced individual gets much from these clinics, if it is but the knowledge that he feels more satisfied with his own methods. I doubt that anybody has come to one of these meetings without a firm conviction that he has gained considerably. At any rate, all practice a better brand of proctology after having attended.

This is the type of society which can bring good proctology within the reach of all practicing physicians and thus to all patients. So, I think that it behooves each one here to take an active part in a functioning society or to help establish a regional group in an area where one does not exist. All of us should never forget that the present relatively good position of proctology is an accolade to those who have preceded us. It is now incumbent upon us to carry on until the ultimate goal of good proctologic care for all is a reality.

Extradural Hematoma of the Posterior Fossa: With Report of a Case

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Another instance of an unusual condition is reported with the suggestion that the EEG may be of diagnostic help.

Introduction

ALTHOUGH extradural hematoma of the posterior fossa has been considered to be relatively rare, the growing number of reported cases indicates the steadily increasing recognition of the condition.[1, 2, 4-8, 11-21, 23-29]

It has been pointed out that missing the diagnosis is usually not so much a matter of differentiation as it is a failure to consider the possibility.[6]

The signs and symptoms of extradural hematoma of the posterior fossa do not constitute a unique syndrome. The classical picture of head injury with unconsciousness, followed by a lucid interval with subsequent deterioration of responsiveness within the next few hours, is absent as often as it is present. Beller's[4] summary of 19 cases shows that only 8 patients lost consciousness immediately after the injury; 14 patients had a lucid interval; 8 patients showed cerebellar signs; 12 patients had noncerebellar lateralizing signs and only 11 patients had x-ray evidence of a skull fracture. Campbell's[6] review of 27 cases stresses the variability of the symptomatology even further. It is not pertinent to review here the various findings in detail since they are so well covered in previous reports.

The purpose of this communication is to report a case of cerebellar extradural hematoma and to describe the electroencephalographic findings.

Case Report

D. L. B., a three and one-half year old white boy, was admitted to the Jackson Memorial Hospital on March 21, 1954, because of drowsiness, irritability and vomiting of two days duration.

He had fallen out of a car without apparent injury except for a small superficial laceration of the left leg. However, during the 48 hours following the accident, he was brought to the emergency room several times by his anxious mother. Each time, except for

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drowsiness, vomiting, and the small laceration noted above, according to the notes, the examination was negative.

Past History. The boy was of normal birth and development. He had had the usual immunizations. He had had measles but there was no history of recent contact with contagious diseases. The family history was negative for diabetes, tuberculosis and hypertension.

Physical Examination. On admission he was drowsy and irritable but well-developed and well-nourished. His blood pressure was 120/80 and the pulse 84; respirations were 20 per minute and regular; the temperature was 98.6°. He was somewhat dehydrated. The general examination was otherwise negative.

There was inability to abduct the left eye completely. There was no papilloedema but the veins of the optic fundi were dilated and markedly tortuous. Motion of the extremities was intact. The sensory pathways were unaffected; the cerebellar tracts were intact and the reflexes were present, equal and active. No abnormal responses could be obtained.

Laboratory Examinations. The blood count and urinalysis were within normal limits. The carbon dioxide combining power of the blood was only 22.1 volumes per cent. Lumbar puncture revealed crystal clear cerebrospinal fluid. The child was not cooperative so an accurate measure of the cerebrospinal fluid pressure was not obtainable. The spinal fluid cell count was 6 lymphocytes per cu. mm. and the total protein was only 5 mg. per 100 cc. Roentgenograms of the skull showed a linear fracture of the occipital bone, just to the right of the midline, extending into the foramen magnum.

Hospital Course. The child was treated for dehydration and electrolyte imbalance and by the next day the CO_2 combining power had risen to 43.8 volumes per cent. On March 22, bilateral abducens weakness was detected. By March 25, the boy was more alert, active and responded better than on admission, and although on March 28, it was the feeling of some of the house staff that the child was markedly improved, the diagnosis of extradural hematoma of the posterior fossa was recorded as a strong possibility. (R.E.S.) Vomiting recurred and by March 31, 12 days after the injury, definite papilloedema was seen for the first time. Electroencephalography on the same date showed generalized, grossly abnormal waves (Fig. 1).

FIG. 1

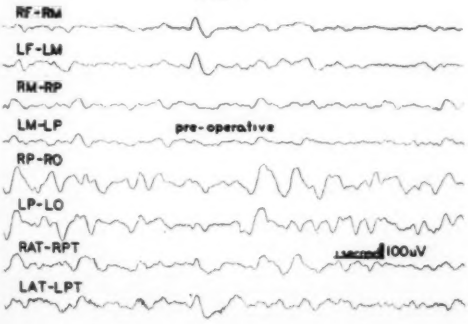
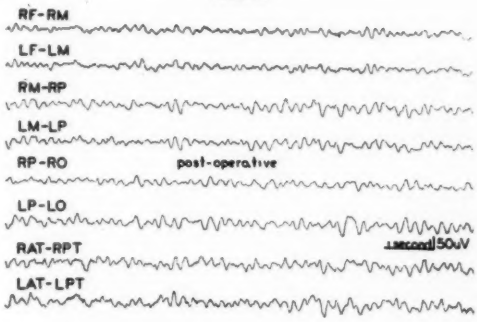


FIG. 2



On April 3, 15 days after injury, a burr hole was placed just to the right of the fracture line and an extradural hematoma, which when completely unroofed measured 3 inches in diameter and almost one inch in thickness at its thickest portion, was completely evacuated. The clot extended both above and below the transverse sinus and across the midline. No active bleeding point was seen.

The child made an uneventful recovery and an electroencephalogram made on the sixth postoperative day was entirely within normal limits (Fig. 2). The papilloedema subsided and the sixth nerve palsies disappeared. The boy was discharged, free of signs and symptoms on April 12, 1954, and has remained so since.

Discussion

Rapid accumulation of blood between the dura and the skull presents the surgeon with a true emergency. However, if the bleeding is from the venous sinuses, where the pressure is low, or if the bleeding is caused by a tear in one of the small terminal branches of the middle meningeal artery, the clot may take some time to form. The distinction between acute and chronic lesions has been noted.[6, 22] In acute cases, the patient shows a rapid onset of signs and symptoms and is either immediately operated on or dies. In the chronic cases, the average length of time between injury and operation (or death) has been about 10 days, although intervals as high as 8 and 9 months have been reported.[5, 26]

Thirty-three cases of extradural hematoma of the posterior fossa have been tabulated for consideration of the time elapsed between injury to operation and survival, injury to operation and death, and injury to death. Of the total number of 33 patients, 20, or 61 per cent, lived more than two days after injury. Of the 19 patients who survived 14, or 74 per cent, were operated on two or more days after injury, and of the 14 who died, 6, or

TABLE 1

SUMMARY OF 33 CASES OF EXTRADURAL HEMATOMA OF THE POSTERIOR FOSSA REPORTED IN THE LITERATURE

Author	*Date*	*Operation* Yes	No	*Time Between Injury and Operation*	*Lived*	*Died*	*Findings at Autopsy*	*Time lived after injury*
Wharton[28]	1901		x			x	x	6 days
	1901		x			x	x	4 days
	1901		x			x	x	a few days
McKenzie[19]	1938*	x				x	x	44 hours
Kessel[16]	1938**	x		48 hours	x			
Coleman and Thomson[7]	1941	x		5 days	x			
Munro and Maltby[19]	1941					x	x	
Gurdjian and Webster[13]	1942	x			x			
Gordy[11]	1948#		x			x	x	12 hours
Grant[12]	1949	x		Less than 24 hours	x			
Bacon[2]	1949	x		12 days	x			
Anderson[1]	1949	x		over 16 days	x			
Turnbull[26]	1949	x		over 9 months	x			
Herren[14]	1950		x			x	x	7 hours
	1950##	x		6 to 8 hours		x	x	2 days post-operative
Wertheimer[27]	1950		x			x	x	14 days
Munslow[20]	1951		x			x	x	12 hours
	1951	x		Probably less than 12 hours		x	x	about 36 hours
Schneider[23]	1951	x		6 days	x			
Bonnal[5]	1951	x		8 months	x			
Christophe[6]	1951	x		33 days	x			
Lemmon[17]	1952	x		12 to 24 hours	x			
Beller[4]	1952	x		over 3 days	x			
	1952+	x		over 7 days		x	x	4 days post-operative
	1952++		x			x	x	36 to 48 hours
Montrieul[21]	1953§	x		13 days	x			
Campbell[6]	1953	x		14 days	x			
	1953	x		6 days	x			
	1953	x		13 days	x			
	1953§§	x		3 hours		x	x	9 hours
	1953	x		36 hours	x			
Saleeby[24]	1954	x		4 hours	x			
Perlmutter, Strain and Feinstein	1954	x		17 days	x			
		24	8		19	14	14	

*The clot was not found at operation.
**Reported in 1942.
#The patient died suddenly before operation.
##Bilateral temporal burr holes showed no clot.
+Clot not found at operation.
++Patient died following lumbar puncture.
§With arachnoid cyst.
§§Subdural hematoma removed. Posterior fossa clot not seen at operation but found at autopsy.

43 per cent, lived two or more days after injury (Table 1).

This summary points up the fact that following head trauma resulting in extradural hematoma of the posterior fossa there is frequently time for diagnostic study. The diagnosis is not always made solely on clinical grounds. Ventriculography, x-ray, lumbar puncture, arteriography and exploratory operative procedures have been used and recommended.

The electroencephalogram has long been recognized as a useful adjunct in the diagnosis of brain disorders of all kinds, including head trauma. However, there is very little as yet in the literature on the EEG findings in patients with extradural hematoma of the posterior fossa.* In 1953, Bonnal[5] reported the

*In 1940, Short[25] reported a case in which the EEG was helpful in localizing an epidural hematoma. However, the clot was not located in the posterior fossa and this case has not been included in the series herein reviewed. Glaser and Sjaardema[10] have also reported on experimental hematoma in animals. Abnormal EEG's were found but no distinction was made between the epidural and subdural lesions in reporting the EEG findings. Williams,[29] in reporting on EEG findings in head trauma also includes nine cases of extradural hematoma. However, he does not mention the location of the clot and these cases are not included in this review.

case of a woman from whom an extradural hematoma of the posterior fossa was removed 9 months after injury. An EEG made 8 months after injury showed depression of electrical activity over the posterior region on the right, failure to follow the flicker stimulus on the right, and a greatly reduced threshold to Metrazol activation. The right posterior localization was confirmed by ventriculography and arteriography.

In view of the fact that a high percentage of patients with lesions in the posterior fossa have abnormal electroencephalograms,[3, 9] it may be expected that patients with an extradural hematoma of the posterior fossa might show similar abnormalities. Especially in those cases showing a delayed onset of signs and symptoms, in the interval between the injury and the development of symptoms, the EEG may be the only objective evidence of brain disease.

In the case described above, the EEG showed a great deal of high voltage, diffuse, 2 to 4 per second activity. In addition, there were frequent bursts of very high voltage 1.5 to 3 per second waves. This activity was not always symmetrical and was somewhat more prominent on the right than the left, but there was no definite localization. In Bonnal's case, the EEG showed a focal depression of electrical activity over the site of the clot.

The incidence of recovery in patients with extradural hematoma of the posterior fossa is rapidly increasing. This is due, undoubtedly, not only to improved surgical technics but to greater awareness of the condition. Prompt diagnosis and surgical intervention is usually followed by recovery. In the series reviewed, of the 24 patients operated on, 20 (87 per cent) survived. Since there is often sufficient time for diagnostic study, the electroencephalogram may prove of value in the early recognition of this condition.

Summary

(1) Electroencephalographic findings in a case of extradural hematoma of the posterior fossa are described.

(2) The importance of electroencephalography in head injury is again emphasized with special reference to extradural hematoma of the posterior fossa.

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Clinical Observations on Allergic Sensitivity to Insulin

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The author reviews a very practical and, at times, a very troublesome subject.

SHORTLY AFTER the discovery of insulin, in 1922, by Banting and Best, there appeared in the literature reports of allergic reactions to the commercially available insulins. Investigation of the validity of these reports is extremely difficult for little attention was given to proper immunologic methods. It was determined that only a few of the reported cases were due to crystalline insulin; most cases were due to the animal protein in the insulin, impurities in the insulin, and perhaps to technic of administration.

The onset of the disturbing symptoms of either a localized cutaneous reaction or a generalized allergy to insulin during the early weeks of insulin therapy are particularly undesirable when one is attempting to get his patient to adjust to a new mode of life. Fortunately, the complication is rarely so severe that insulin therapy must be stopped. With newer types of insulin and more refined methods of preparation, the incidence of all types of allergy to insulin is decreasing.

Long acting insulins were reputed not to produce cutaneous reaction. Kern and Langner,[1] in 1939, found in 104 patients receiving protamine zinc insulin, that 16 per cent of cases had a reaction manifested by redness and swelling at the local site of injection. Similar claims for globin and NPH (modified protamine insulin) insulins have also been made but proven untrue. Reactions were less frequent and least severe with crystalline and recrystallized insulins (6x) than with commercial preparations (Paley).[2]

It has been said that the frequency and tendency of the various insulin preparations with reference to their ability to cause reactions may be listed in the following order:

1. Protamine zinc insulin
2. Protamine insulin mixtures
3. Globin insulin
4. Regular insulin
5. Zinc insulin crystals
6. NPH (neutral protamine Hagedorn)
7. Lente insulin
8. Crystalline and recrystallized insulins

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Incidence

The reported incidence of allergic sensitivity to insulin varies from less than 1 to 55.8 per cent (Paley-Leeds General Hospital).[2] Hallerman[3] in a series of 541 patients treated with insulin found only two cases of sensitivity severe enough to warrant discontinuation of therapy.

Allen and Scherer[4] state that only 1 to 2 per cent of all cases sensitive to insulin will show systemic reactions manifested by urticaria, pallor, angioneurotic edema, hypotension, circulatory collapse, joint pains, and gastrointestinal symptoms. The other 98 to 99 per cent manifested only mild to severe local reactions. Most of these local reactions came on seven to ten days after the start of insulin therapy and disappeared after a few days to to a few weeks. This desensitization occurs spontaneously and may be expected to occur in most of the mild local reactions.

One interesting point raised by Yasuna[5] shows the highest incidence of allergic reaction to insulin in the older age groups. Since this group routinely has the milder type of diabetes, treatment by diet without insulin is more feasible than in the younger diabetic.

In the diabetic clinic of the General Infirmary at Leeds, 55.8 per cent of 147 patients starting insulin therapy during 1947-49 developed cutaneous reactions.[2] The reaction was mild in 81.7 per cent,—immediate in 74.4 per cent, delayed in 7.3 per cent; and severe in 18.3 per cent,—immediate in 17.1 per cent,

delayed in 1.2 per cent. Although the delayed reactions are less common they are the most severe. In view of statistics such as these we feel the problem has some practical as well as theoretical interest.

Mechanism of Allergic Reaction

The mild local reactions at the site of the injection usually consist of erythema and slight induration which disappears in 24 to 72 hours. These reactions are probably non-immunologic and are of little clinical significance.

The severe local reactions are conceivably due to sensitivity to animal protein rather than to the insulin itself. Several cases of this type reaction were proven cases of atopy.

The severe general reactions are definitely an antigen-antibody type of reaction. The reagins for insulin can be found in cases with severe constitutional reaction. Passive transfer tests can be demonstrated. The resemblance of some of the more severe type of insulin reactions to serum sickness, particularly with regard to the latent period, have been pointed out by many observers.[6, 7]

Wasserman and Mirsky[8] offered experimental confirmation of allergic sensitization to insulin itself. Animals sensitized to beef insulin were shocked by pork, sheep and bison insulin. Parallel complement-fixation reactions were obtained.

It may be well here to point out an interesting and unsolved medical problem. Does some antagonism exist between diabetes mellitus and allergy? Gutmann[9] points out that a review of literature reveals only 35 cases of bronchial asthma in 19,126 diabetics. In his private practice of 2,000 patients having allergic diseases, he had only five diabetics. The usual incidence in the country at large is 3 in 100. On the other hand, in a group of 40 severe diabetics whose insulin requirements were from 50 to 110 units per day, Siegal and Herzstein[10] found eight to have clinical manifest or latent atopy. An almost identical incidence of atopy (20.7 per cent) was found in parallel observations in a nondiabetic control group of 227 patients, 47 of whom had clinical or latent atopy. These observations would indicate that there exists no special relationship between the two hereditary states of atopy and diabetes mellitus. Patients with severe diabetes have not been shown to have any unusual predisposition to atopy. It appears most unlikely that diabetes mellitus of the more severe variety is based on any immunologic mechanism, such as seems to occur in rare instances of insulin resistance and allergy.

Types of Reaction

Reactions to insulin may be grouped into four categories: (1) mild local reactions; (2) severe local reactions; (3) systemic reactions; and (4) miscellaneous,—insulin lumps, lipodystrophy, and so on.

1. The *mild local reaction* at the site of injection is the most frequent type of allergic reaction to insulin. These are localized, self-limited and will generally disappear in a short time with continued administration of insulin. This has been called "automatic self-desensitization." Clinically, this reaction is manifested by a stinging, burning or itching sensation at the site of the injection. In one-half to three hours this area will become mildly indurated. The area of induration may be surrounded by an area of erythema and in most cases is painful. This type of reaction lasts from one to three days.

2. The *severe local reactions* which occur at the site of the injection consist of an accentuation of the mild local reaction. The area of erythema and induration measures up to 10 cm. or more in diameter. These indurations may develop into sterile abscesses and may require incision and drainage. These reactions may be immediate or delayed, the latter being the most severe. In addition, there is a variety of local reaction manifested by superficial urticaria localized to the site of the injection. Three patients with this symptom have been reported to be atopic.

3. *Systemic reactions* are fortunately much less common but they are far more spectacular. This type generally comes on within one-half hour of the injection and may disappear spontaneously after an hour. This type of reaction is due to an allergic reaction to the insulin protein itself. These reactions do not come on during the early days of insulin therapy, but only after several weeks of treatment or after renewal of insulin therapy following a lapse of several months or years.

This systemic reaction is manifested by angioneurotic edema, asthmatic wheezing, ab-

dominal cramps, arthralgia, laryngeal stridor, cutaneous eruptions, urticaria, hypotension and circulatory collapse. This type of response naturally interrupts treatment of the diabetic and calls for prompt treatment of the insulin hypersensitivity.

The appearance or disappearance of allergic reactions to insulin in no way interferes with the physiologic activity of insulin. Nondiabetic persons may develop the same type of reactions described above.

4. *Miscellaneous types of reaction.* Lipodystrophy represents an atrophy of subcutaneous fat. It is most common in children of both sexes, occasionally is seen in adult females and almost never in adult males. The lesion almost always occurs at the sites of injection, although in rare instances it is seen in remote areas. The incidence is reported by Marble and Smith[11] to be 18.4 per cent in 500 cases. The atrophy has been ascribed to the tricresol preservative, lipase content of insulin, trauma, low grade infection, nerve injury, antiseptics, androgen insufficiency, active local oxidation or carbohydrate which causes local combustion of fat. Most of these have been refuted and the actual cause is still obscure. If injections are discontinued in the involved area, there will be spontaneous regeneration of subcutaneous tissue in two to eight years. Bartelheimer[12] reports a 27 year old male who was a known diabetic for 10 years. He developed lesions which represented a variant case of lipodystrophy, which began three months after the beginning of insulin therapy.

Treatment

The treatment of the mild local reactions consists simply of reassuring the patient that the symptoms will subside spontaneously in a few weeks.

Technic of injection should be checked to see if the following points are being observed:

(1) the site of injection being alternated to advantage; (2) avoidance of excessive rubbing of skin prior to injection; (3) avoidance of injection of insulin into skin; (4) symptoms may be relieved by the use of separate needles for withdrawing and injecting insulin.

Antihistamines may be of value in the more persistent local reactions. An antihistaminic cream may be used on the injection site prior to injection. Use of 0.5 to 1.0 cc. Benadryl solution with the injection of insulin may be helpful. Oral antihistaminic therapy is least effective in control of cutaneous reactions.

When the allergy is proven to be due to other than the insulin protein factor, a change in the product or use of crystalline insulin will eliminate the problem. This includes the use of insulin from a different animal source. Insulins from several animal sources are commercially available.

When the allergy is due to the protein in the insulin itself, there are only two courses open, namely, treatment by diet alone or desensitization to insulin.

Many methods of desensitization have been proposed. That, of Corcoran,[13] is most useful. Three dilutions of crystalline zinc insulin are made,—1:1000, 1:100, 1:10. Beginning with the weakest dilution, 0.1 cc. is administered initially followed by an increase of 0.1 cc. every hour until 1 cc. of that dilution is given. Then the stronger solutions are given in like manner finishing with undiluted insulin, 0.1 cc. (4 units) every hour, until the desired therapeutic effect of insulin is obtained. After this desensitization program is completed, any type of insulin indicated may be given without danger.

When no emergency exists, one may use the method of Joslin[14] for slow desensitization. He uses 1/1000 unit before breakfast, 1/500 before lunch, 1/250 unit before supper, 1/125 before retiring. On the second day, doses of 1/100, 1/50, 1/25 and 1/12 unit are given. On the third day 1/5, 1/2, 1, and 2 units are given, and so on until a therapeutic response is obtained.

Skeptophylactic de-allergization (Urbach[15]). This method devised by Urbach employs the administration of 1/2 to 1 unit of insulin subcutaneously 45 minutes before the main injection of insulin. This method differs from hyposensitization in that it is a method where clinical sensitivity is due to the production of an excess of free circulating antibodies by the repeated administration of small doses of antigen. The neutralization of the antibodies that follows results in clinical insensitivity. Failure was reported when this method was used, so Hughes[16] in his case reduced the preadministration dose to 0.0001 unit and gave it intradermally rather than subcutaneously.

There are three other methods of treating insulin hypersensitivity. Hughes[16] has used Hapamine injections successfully. Collens,

Lerner and Fialka[7] employed histamine phosphate beginning with 0.1 mg. and gradually increasing the dose to 1.0 mg.

Finally, Dolger[17] has shown that insulin may be boiled for three hours and still retain 1/2 of its potency. Boiling for 15 minutes will cause a loss of only 10 to 20 per cent of its physiologic activity. Dolger used this denatured insulin for a case of severe insulin hypersensitivity and also for the more serious cases of cutaneous reactions to insulin.

Summary

We have seen that insulin hypersensitivity is a common clinical entity. Fortunately, the great majority of these cases are self-limited and no treatment except reassurance is indicated. When a systemic reaction does occur, several proven and available therapeutic courses may be followed. These therapeutic methods have been enumerated.

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A New Therapeutic Approach to Certain Cases of Alcoholism

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The effect of a new drug in a condition in which psychotherapy may play a large part is always difficult of evaluation. A report such as this deserves numerous and broad studies for confirmation.

FOR YEARS CLINICIANS HAVE SEARCHED for some chemical means of treating alcoholic patients. In the past two decades many drugs have been utilized in the therapy of alcoholism. No one drug has been beneficial in all patients, and it is doubtful that one ever will be because of the variation in the psychopathology of alcoholism. Primarily, alcoholism is not an illness *per se* but, rather, it is a symptom of some underlying disorder. As the underlying disorder may vary from one patient to another, so the treatment must vary if it is to be successful.

This report is based on a series of 40 patients whose alcoholism was a symptom of underlying depression. Depression is an elusive disorder with many ramifications, and it is frequently masked by numerous symptoms. All are familiar with the patient who verbalizes many somatic complaints without organic cause, while the basic disorder is an involutional depressive reaction.

The Drug Meratran

Recently a new "mood lifter," or central

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nervous system stimulant, has become available for therapeutic trial. Meratran (alpha-((2-piperidyl)) benzhydrol hydrochloride)† has been used clinically since 1953. The experimental work of Brown and Werner[1] revealed the drug to be low in toxicity in both acute and chronic toxicologic experiments. No convulsions occurred until lethal doses were given intravenously, and doses of the compound which caused hyperactivity in the experimental animal had little or no effect on blood pressure, pulse rate or respiratory rate.

Because of these considerations Fabing[2] began to use the drug experimentally in clinical trials. He found Meratran useful in treating narcolepsy and reported on over 100 cases with this disorder. He found no diminution of appetite, little or no interference with nocturnal sleep, no alteration in blood pressure, pulse rate, respiratory rate, or pupillary size. He also utilized the drug successfully in treating several cases of blepharospasm and spasmodic torticollis.[3]

Many other investigators have since studied this drug. Schut and Himwich[4] studied its effects on hospitalized patients at the State Research Hospital in Galesburg, Illinois. They discovered, in a "double blind" study, that Meratran was valuable in treating nondeluded schizophrenics having restriction of interest and activity and with depressant features, in psychomotor retardation and/or blocking of communication, and in long term hospitalized schizophrenics with severe deterioration.

Pomeranze[5] found the drug useful in treating geriatric patients with depressive symptoms associated with premature retirement and fear of impending deterioration and death. He found it safe to administer and its use did not produce untoward side effects. Levy[6] utilized this compound in treating depressive reactions of the office practice type with encouraging results. Antos[7] has used Meratran in numerous disorders to relieve fatigue and elevate mood in cases where amphetamine preparations might be contraindicated, such as in diabetics or patients with hypertension or other cardiovascular disorders.

†Meratran is the trade-name of the Wm. S. Merrell Company for its brand of pipradrol (alpha– ((2-piperidyl)) benzhydrol hydrochloride). Investigational supplies were provided by the Medical Research Department, the Wm. S. Merrell Company, Cincinnati 15, Ohio.

Mode of Action

The mode of action of Meratran has been fairly well established by a number of competent investigators. Its action is not mediated by the autonomic nervous system and it seems to be a true central nervous system stimulant. Renaldi and Himwich[8] found that in the rabbit the subcortical area responsible for the alerting reaction, namely the reticular substance of the upper brain stem tegmentum, was stimulated by Meratran. Himwich also states: "Though Meratran is a stimulant and therefore resembles amphetamine in some of its action, it does not belong to the group of sympathomimetic drugs, for it does not evoke the overactivity of the sympathetic nervous system characterized by dilated pupils, sweating, fast heart rate, and increased blood pressure." Heath[9] found that Meratran given intravenously to monkeys produced in electroencephalograms rapid high voltage spikes, with the electrodes implanted in the septal area.

The author became interested in Meratran when the possibility was presented of utilizing it in alcoholic patients. A preliminary report on its use in this disorder was presented several months ago.[10] As previously stated, this report deals with 40 alcoholic patients who showed depression as an associated syndrome.

Results

Patients were selected carefully for this study on the basis of psychiatric history, past medical history and, in many instances, psychologic tests. Particular attention was paid to those patients who had periodic alcoholic bouts and who expressed the opinion that their drinking was precipitated by feelings of depression. In most of these patients, psychologic tests and interviews with their families corroborated their own opinion that their alcoholic bouts were precipitated by depression. The group was made up of 25 men and 15 women, with an age variation of from 25 to 60. The course of these patients has been followed for a period of about 12 months.

The results have been gratifying for this period of time. Of the 25 men, 18 have remained sober. Of the 7 who did not remain sober, 3 had only one alcoholic episode during the 12 months, while 4 had two or more such episodes.

The results among the 15 women showed that 10 remained sober during the year, one had only one alcoholic episode, and 4 had two or more.

Discussion

Initially one must recognize that a large part of the ability of these patients to remain sober was due to psychologic factors. A certain rapport was established between the therapist and the patients. Also, not enough time has passed to adequately evaluate the drug as a useful agent in treating alcoholic patients. However, formerly a much smaller percentage of such patients would have remained sober for 12 months than did those using the medication. Some of the patients were given Meratran and instructed to take it when they felt themselves becoming depressed. The usual dosage was 2 mg. twice a day. Other patients were seen at regular intervals during the year and when depression seemed to be developing, Meratran was prescribed in doses ranging from 2 to 8 mg. per day in divided doses. The medication was given for about a ten day period of time, and when it was discontinued, no withdrawal effects nor a "let down" were felt by the patients nor noted by the physician. No patient had to take the medication more than six times during the 12 month period, and the average was four.

Case Report

Mrs. K. L. B., a 42 year old married housewife, had a history of chaotic alcoholism for the past 10 years.

She is a woman who has always been interested in community activities and took an active part in them and in her church work. She had been a member of Alcoholics Anonymous for several years but recently had lost interest in this work and felt that she could no longer continue in it. She had had considerable question in her mind for several years as to whether or not she was a true alcoholic.

Her psychiatric history revealed that for the past 10 or 12 years she had had recurring episodes of mild to moderate depression. She would first begin to lose interest in her family (her husband and three children), and in her housework and activities. She would have numerous somatic complaints concerning tension, headaches, and difficulty in sleeping, but her main complaint was mild depression and loss of interest. The depression would become progressively worse until such time as she would spend a great deal of time in bed or in her room reading. She took very little interest in her appearance, in her family, and in her surroundings, and this type of reaction would generally terminate in an alcoholic "binge" which would last for several days. On some occasions it became necessary for her to be hospitalized, but in most instances her family physician was able to bring her out of the alcoholic state at home. She might then continue to drink a little for a week or so. There is a history of one suicidal attempt, considered to be genuine.

The patient was seen for psychiatric treatment and some rapport was established. She was placed on a dosage of Meratran 2 mg. twice a day, to be taken when she felt the depression coming on. She was allowed, in the main, to regulate her own dosage of the medication.

Since this regimen has been set up, the patient has remained sober for approximately a year. Prior to this she would have had at least four to six alcoholic binges in a 12 month period of time. At the present time, when she notes the onset of depression, apathy, and lack of interest and energy, she takes Meratran for approximately 10 days to 2 weeks in the above-mentioned dosage, and it has not been necessary for her to resort to alcohol as a release from a depressive state.

Summary and Conclusions

Meratran, a new central nervous system stimulant, is discussed from a historical, chemical, and experimental standpoint. Forty cases of patients with periodic alcoholism precipitated by depression are presented. It is concluded that in some carefully selected cases of alcoholism, where this is a symptom of depression, Meratran may be a useful tool to use with other methods of treatment, particularly psychotherapy.

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UP TO THE PRESENT

Treatment of Hypertension: Part III.

Pharmacodynamics in Therapy: Peripherally Acting Agents*

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IN THE PREVIOUS PAPERS on the therapy of hypertension we discussed the rationale for agents which act centrally to suppress abnormal vasoconstrictor impulses. We also discussed the use of agents which block vasoconstrictor impulses at either the ganglion or the neuro-effector site in conjunction with central depressants such as Rauwolfia, hydralazine, or veratrum.

The present discussion comprises a more detailed description of ganglionic and adrenergic blocking agents and an over-all approach to the treatment of clinical hypertension which we have found helpful.

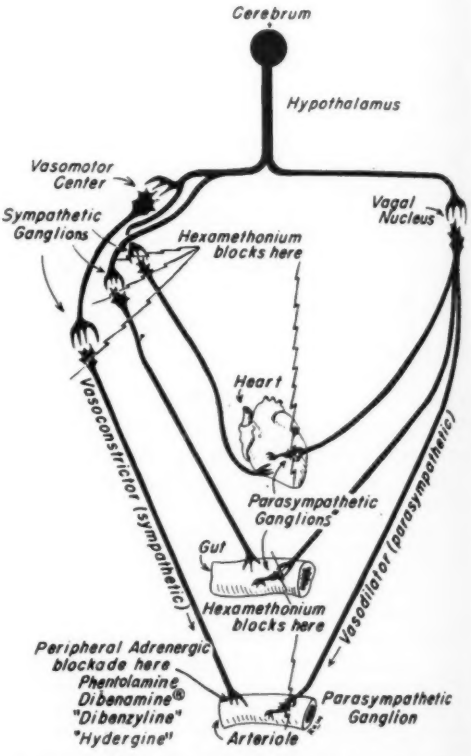
Ganglionic Blocking Agents

Three ganglionic blocking agents are currently used in the treatment of hypertension: hexamethonium, pentolinium and mecamylamine. Of the three, only mecamylamine is completely absorbed when administered orally. All three agents interfere with reflexes responsible for the postural adjustment of blood pressure. Thus, the maximal blood pressure reduction is in the blood pressure taken in the upright position. Since all three produce a blockade of sympathetic and parasympathetic ganglia (Fig. 12), their side effects include constipation, urinary difficulties, dryness of the mouth, postural dizziness, and even syncope.

HEXAMETHONIUM. This is a bismethonium compound composed of two ammonium radicals united by a chain of six methyl groups (Fig. 13) for which the compound is named.

Pharmacodynamics. Hexamethonium reduces blood pressure by blockading vasoconstricter impulses at the sympathetic ganglia. By inhibiting the reflexes initiated by postural

FIG. 12



Diagramatic representation of the autonomic nervous system. When ganglionic blocking agents such as hexamethonium are administered, both the ganglia of the sympathetic as well as the parasympathetic nervous system, are blocked. The effect on any one tissue inervated by the autonomic nervous system will depend on whether the sympathetic or the parasympathetic component of this system was motor. Thus, the effect of ganglionic blockade on the blood vessel will be primarily the effect of blocking the sympathetic nervous system whereas the effect on the gut will be primarily the effect of blocking the parasympathetic nervous system. As a result, the blood pressure is reduced and at the same time, gastrointestinal motility is decreased.

*Supported in part by a grant from the Houston Heart Association.

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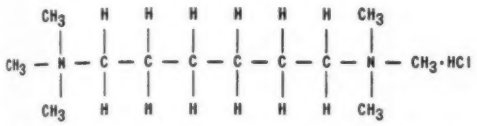
FIG. 13

STRUCTURAL FORMULA OF HEXAMETHONIUM



Structural formula of hexamethonium. The drug obtains its name from the number of carbon atoms between the two nitrogens. If this chain of carbon atoms is increased to ten (decamethonium) then the compound loses its ganglionic blocking properties and it becomes a curare-like agent.

change, it produces a reduction in orthostatic blood pressure. Tachycardia does not occur since the cardio-accelerator reflexes initiated by an acute drop in blood pressure are also blocked. Because the hexamethonium blockade is ganglionic, norepinephrine will reverse excessive hypotension.

Cerebral Hemodynamics. When the blood pressure is reduced, the cerebral vessels dilate and cerebral blood flow is maintained. Excessive reduction, however, may diminish cerebral blood flow and produce dizziness or syncope (Fig. 4).

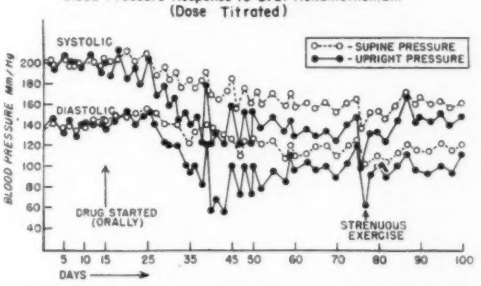
Renal Hemodynamics. Initially acute reduction of blood pressure may depress renal function (Fig. 5). However, if the reduction is not too great, or too sudden, the glomerular filtration rate will return to the control level despite a maintained reduction in blood pressure.[51] Since patients with renal damage readjust more slowly, excessive reduction of their blood pressure is contraindicated. To prevent renal decompensation in these patients, the standing blood pressure should not be reduced below the upper normal limits.

Side Effects. Three categories of untoward effects are associated with hexamethonium therapy: (1) weakness and fatigue; (2) constipation, urinary retention, dry mouth, blurring of vision, anorexia, and impotency; (3) excessive hypotension produced by sympathetic ganglionic blockage and characterized by orthostatic dizziness and syncope, and blurring of vision. These untoward effects are less prominent when hexamethonium is used in conjunction with Rauwolfia, since less hexamethonium is required[52] (Fig. 19c).

Clinical Use. Hexamethonium is effective orally and parenterally. The most marked effect occurs when the patient is erect.

FIG. 14

Blood Pressure Response to Oral Hexamethonium (Dose Titrated)



Blood pressure response to dose adjustment of the ganglionic blocking agent. As the dose is progressively increased over a period of four weeks, the blood pressure is reduced to the desired level. The reduction in blood pressure is primarily in the orthostatic position. Strenuous exercise and hot weather increase the effectiveness of ganglionic blocking agents.

Oral Therapy. Until several years ago, hexamethonium was used alone in the management of hypertension. Today, however, because its high response rate was obtained only at the expense of a high incidence of untoward effects, it has become practice to use hexamethonium only in conjunction with a less potent central agent such as Rauwolfia.

Whether used alone or together with other agents, hexamethonium is given in small doses, 125 mg. four times daily (after meals and at bedtime). The dosage is increased by titration until either an optimal reduction of the blood pressure is obtained, or until untoward symptoms prevent further increase in dosage. Since exercise (Fig. 14) and hot weather increase the response to hexamethonium, the dosage may have to be varied according to the patient's activity and the season of the year.

In addition to observing the blood pressure, prevention of the clinical manifestations of excessive hypotension, such as dizziness or syncope on standing, should be considered in

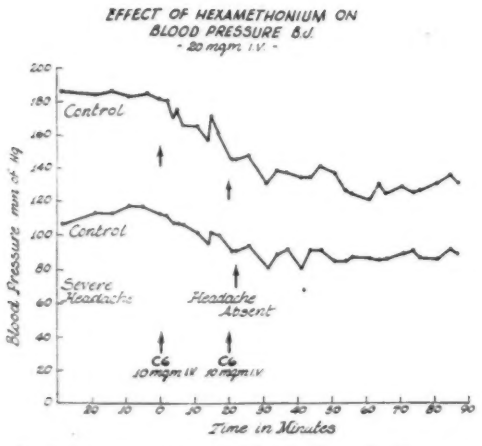
TABLE 1

AN EXAMPLE OF DRUG TITRATION FOR ESTABLISHING THE PROPER DOSE FOR EACH PATIENT[27]

	Dosage of Hexamethonium			
	7 a.m.	*12 noon*	*5 p.m.*	*10 p.m.*
1st week	125 mg.	125 mg.	125 mg.	125 mg.
2nd week	250 mg.	250 mg.	250 mg.	250 mg.
3rd week	500 mg.	250 mg.	250 mg.	500 mg.
4th week	500 mg.	500 mg.	500 mg.	500 mg.
5th week	750 mg.	500 mg.	500 mg.	750 mg.

Note: Dose is maintained constant at whatever level an adequate reduction in blood pressure is obtained.

FIG. 15



Blood pressure response to parenteral hexamethonium in a patient with malignant hypertension. The blood pressure is lowered within a matter of minutes after parenteral administration of this drug.

planning dosage schedules. Constipation, commonly associated with the hexamethonium ganglionic blockade, must be controlled (e.g. with prostigmine, 15 mg. before each meal) if the absorption of hexamethonium from the gastrointestinal tract is to be kept constant.

The most important limiting factors of hexamethonium therapy are its transient effect and inconsistent (and poor) absorption from the gastrointestinal tract. It is important to note that patients with severe disease and those with relatively mild disease (Table 2) respond equally as well.

Parenteral Therapy. This will be discussed in greater detail in a future article. In general, hexamethonium may be given either intramuscularly or intravenously. Intramuscularly, the initial dosage is 10 to 15 mg. every 4 to 6 hours with gradual increases until an optimum effect is obtained. Intravenously, 100 mg. of hexamethonium may be diluted in a liter of fluid with the infusion speed determined by the response.

TABLE 2

RESPONSE OF BLOOD PRESSURE TO GANGLIONIC BLOCKADE (HEXAMETHONIUM)[52]

Drug	*Number Patients Treated*	*Responsive*	*Normotensive BP<150/100*
Hexamethonium			
Group 1*	29	86%	31%
Group 2*	58	84%	38%
Group 3*	33	88%	20%
Total	120	86%	32%

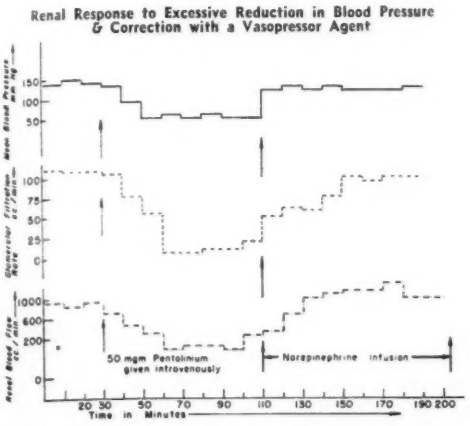
*Control diastolic pressure for Group 1 was more than 100 mm. Hg. but less than 120 mm. Hg.; Group 2 more than 120 but less than 140; Group 3 more than 140 mm. Hg.

PENTOLINIUM, PENTAPYRROLIDINIUM (ANSOLYSEN, M & B 2050). Pentolinium is a new ganglionic blocking agent recently synthesized by Libman, Pain, and Slack.[53] It has been reported to be more potent than hexamethonium on a milligram for milligram basis, and to have a longer duration of action.[54]

Pharmacodynamics. In general, the pharmacologic effects of pentolinium are similar to hexamethonium. Impulses are blocked at both sympathetic and parasympathetic ganglia (Fig. 6). The blood pressure reduction produced by pentolinium is orthostatic and dosage should be regulated according to the upright blood pressure. Orthostatic dizziness and syncope may be anticipated, as well as constipation, urinary retention, dry mouth, blurring of vision, and impotence produced by parasympathetic ganglionic blockade. Because of its ganglionic site of action, norepinephrine effectively reverses excessive pentolinium—induced hypotension. Smirk[55] has reported that "insofar as they have been examined, the effects of pentapyrrolidinium on the circulation appear to be identical with those of hexamethonium but the dose is smaller and the duration of action longer with the pentapyrrolidinium." He suggests that the duration of action of pentolinium is 8 to 12 hours or more, in comparison to 2 to 4 hours with oral hexamethonium. Both are excreted primarily through the kidneys. As with hexamethonium, pentolinium absorption is poor and inconsistent. Roughly 10 to 20 times the subcutaneous dose must be given orally to achieve the same effect. Freis[54] reported the mean effective parenteral dose of pentolinium was 15 mg., whereas the mean effective oral dose was 280 mg. The onset of action is about one hour after oral administration. Some degree of tolerance to parenteral therapy was noted, but this was not so marked as with hexamethonium.

In comparing renal hemodynamic responses to parenterally administered pentolinium we found the onset of action to be much more rapid following single intravenous injections than following continuous infusions. After one hour, the renal hemodynamic effects of the two methods were similar. After two or

FIG. 16



Renal hemodynamic response in a patient who obtained an excessive reduction in blood pressure with pentolinium. When this occurs, the glomerular filtration rate and renal blood flow are markedly reduced. However, this is easily corrected by merely raising the blood pressure with any vasopressor agent such as norepinephrine, Neosynephrine or Aramine.

three hours, however, the glomerular filtration rate and renal blood flow rose toward the control levels following single intravenous injections. Final depression was at about the same degree as the initial depression during the continuous intravenous infusions.

A reduction in sodium and water excretion paralleled the reduction in glomerular filtration rate and renal blood flow. There was also an insignificant reduction in potassium excretion. These alterations of renal hemodynamics, and water and electrolyte excretion rates occurred within normotensive ranges and were greater than those observed in the normotensive subjects in whom the blood pressure was reduced to hypotensive levels.

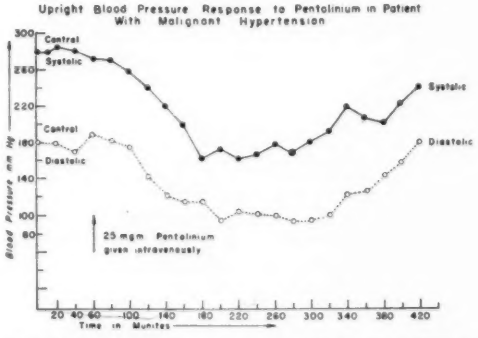
The renal hemodynamic response to blood pressure reduction by continuous infusions of pentolinium and hexamethonium was the same. The depression in water and electrolyte excretion following intravenous infusions of these drugs was similar.

Following oral administration of pentolinium for three months or more, renal hemodynamic readjustment was observed when patients were supine and renal vasoconstriction occurred when they were erect. Thus, the glomerular filtration rate and renal blood flow were the same as before pentolinium therapy. When pentolinium caused an excessive reduction in blood pressure, the glomerular filtration rate fell markedly and anuria developed. This complication was quickly reversed with norepinephrine (Fig. 16).

Clinical Use. The general principles of hexamethonium and pentolinium treatment are the same. Pentolinium is approximately 10 times more potent milligram for milligram and has a longer duration of action. However, as Wilkins[56] points out, and as is true of all pharmacologic agents, some of the advantages derived from the use of a new drug may actually be due to the increasing skill of the physicians who use them. Pentolinium dosage is started in a low range, 20 mg. given four times daily and increased by titration. Dosage should depend upon the blood pressure in the upright position. Symptoms of excessive hypotension are evidence of excessive dosage. Smirk[55] believes an almost optimal blood pressure response may be obtained by increasing the dosage of pentolinium a small amount with each succeeding dose until the patient becomes faint if he stands at the time of the maximal drug effect. According to Smirk, the ideal dose is approximately 20 mg. less than the dosage which will produce this reaction. This, however, is not generally accepted, since, at this dosage, the patient may, without warning, have frank syncopal episodes.

Freis[54] has noted extraneous factors which influence blood pressure response to pentolinium and which might also influence the response to hexamethonium, mecamylamine, or adrenergic blockade. Factors which increase the hypotensive response to pentolinium in-

FIG. 17



Upright blood pressure response in a patient with malignant hypertension. There is more of a delay in response to pentolinium than that which is observed after the administration of hexamethonium. However, the maximum reduction in blood pressure is comparable and the length of action of pentolinium is considerably greater than that of hexamethonium.

clude: (1) ingestion of alcohol or a large meal; (2) vigorous exercise (in contradistinction to the rise after exercise in untreated hypertension or normotensive patients); and (3) hot summer weather.

Freis used oral pentolinium alone as the sole hypotensive agent in 27 patients for from 2 to 6 months. Medication was given every 8 hours. The mean daily effective dose was 300 mg. of the ion. At that level, 85 per cent of his patients obtained a diastolic pressure reduction of at least 20 mm. Hg. in the average standing blood pressure. Gifford[57] reports similar findings in a study of eight previously untreated patients who received only pentolinium. The average fall in the standing diastolic blood pressure for these patients was 30 mm. Hg.

Freis[54] noted that pentolinium given intravenously took at least 10 minutes to produce a maximal effect. This delay in response may be even more prolonged (Fig. 17). Hexamethonium, on the other hand, works almost instantaneously, making it much easier to use. The mean effective subcutaneous dose of pentolinium was 15 mg. per day, or about one twentieth the hexamethonium dosage.

Constipation must be avoided in pentolinium therapy. If necessary, prostigmine may be given regularly in doses of 15 to 90 mg. per day.

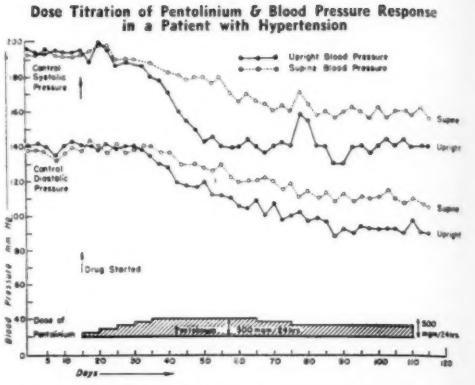
A combination of pentolinium and Rauwolfia was tried on patients unresponsive to Rauwolfia alone and in patients with severe or rapidly progressive hypertension. Seventy-five patients unselected except that they had previously received Rauwolfia and hexamethonium, were given Rauwolfia plus pentolinium. The two regimens produced comparable rates of response and untoward effects (Table 3).

TABLE 3

COMPARISON OF BLOOD PRESSURE RESPONSE—MECAMYLAMINE, HEXAMETHONIUM AND PENTOLINIUM[23]

	Rauwolfia + Mecamylamine		*Rauwolfia + Hexamethonium*		*Rauwolfia + Pentolinium*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Number patients treated	50	100	75	100	75	100
Responsive	46	92	57	76	59	79
Normotensive	12	24	28	37	25	33
Unresponsive	4	8	18	24	16	21
Avg. dose of responders	17 mg.		2307 mg.		341 mg.	

FIG. 18, A

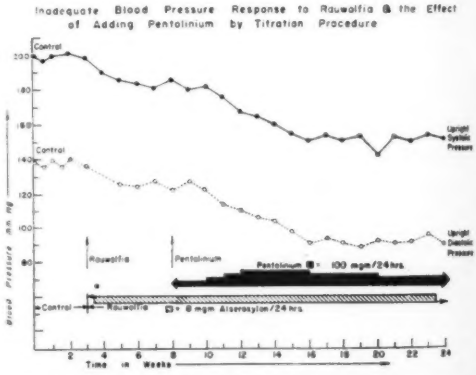


Dose titration of pentolinium in a patient with severe hypertension. As the dose is progressively increased, the blood pressure is reduced but the reduction is primarily in the orthostatic position.

Summary: Hexamethonium and Pentolinium. (1) Both hexamethonium and pentolinium act at the sympathetic ganglia to block vasoconstrictor impulses and thereby reduce the blood pressure. The major effect is on the orthostatic blood pressure suggesting that the extent of this effect must be used as a guide for regulating dosage.

(2) Both agents block parasympathetic ganglia as well as sympathetic. The parasympathetic block may cause constipation, impotence, and occasionally, urinary retention. The sympathetic block may result in orthostatic dizziness and syncope.

FIG. 18, B



Blood pressure response in a patient who was receiving combined Rauwolfia and pentolinium. The blood pressure response to Rauwolfia alone was significant but inadequate. Then as pentolinium was added and the dose was progressively increased, the blood pressure was further reduced to the desired level.

(3) Oral administration may be employed with hexamethonium and pentolinium. Response is proportional to dose, necessitating the use of a titration method for arriving at each patient's optimal dose.

(4) Excessive hypotension must be avoided.

(5) Pentolinium appears to be about eight to ten times as potent as hexamethonium on a milligram for milligram basis, and its duration of effect is longer.

(6) A smoother effect may be obtained when hexamethonium or pentolinium is used with Rauwolfia (Fig. 18 B). In combined therapy the required dose of the ganglionic blocking agent is less and there is a proportionate decrease in untoward effects and increase in the response rate.

MECAMYLAMINE. The most potent ganglionic blocking agent now available is mecamylamine. A crystalline synthetic compound, it is the first ganglionic blocking agent to be introduced which is not a quaternary ammonium compound.

Pharmacodynamics. Mecamylamine produces a blockade of both sympathetic and parasympathetic ganglia. Experimentally, it produces the same cardiovascular and renal hemodynamic effects observed with hexamethonium and pentolinium. The orthostatic blood pressure reduction it induces may be readily combatted by norepinephrine.

The most unique and clinically desirable attribute of mecamylamine is its almost complete absorption from the gastrointestinal tract. A preliminary report of experimental toxicity studies by Karl H. Beyer, Jr., established that the LD 50 by oral and subcutaneous routes was the same. Thus, the day-to-day variation in blood pressure response, depending on absorption, should be minimized in mecamylamine therapy. Experimentally and clinically, the ganglionic blockade of mecamylamine is longer than that of either hexamethonium or pentolinium. Experimentally, the effect on the nictitating membranes was found to be 10 to 20 times as prolonged as that of hexamethonium and 3 to 4 times that of pentolinium.

Clinical Results. We have used mecamylamine on a clinical trial basis for about four months.[58] A large group of patients who were formerly on Rauwolfia plus pentolinium were changed to Rauwolfia plus mecamylamine with a substantial improvement in response rate. Patients previously untreated have been given mecamylamine alone.

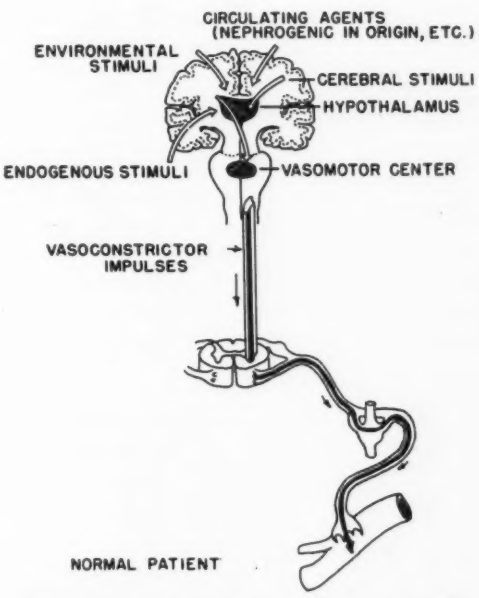
The drug's long action and complete absorption gave a more predictable and constant reduction of blood pressure which could be maintained from day to day. Patients had marked reduction in blood pressure without syncope because of the gradual onset and stability of the reduction. Rauwolfia gives additional support to the effectiveness of mecamylamine and this combination may prove to be

TABLE 4

UNTOWARD EFFECTS—HEXAMETHONIUM AND PENTOLINIUM[23]

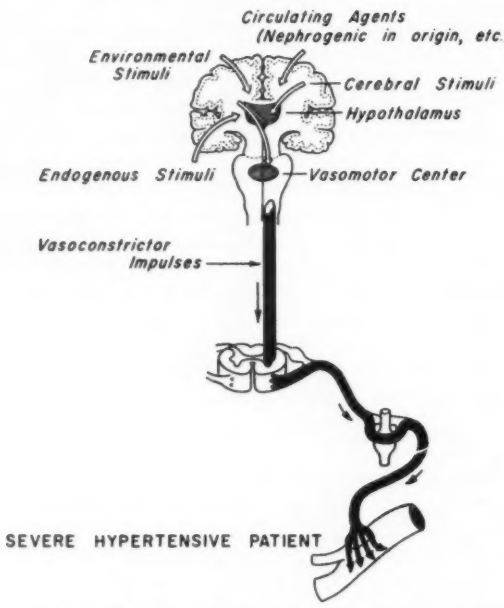
	Rauwolfia + *Pentolinium (Per Cent)*	*Rauwolfia* + *Hexamethonium (Per Cent)*	*Rauwolfia* + *Mecamylamine (Per Cent)*
Bradycardia	67	68	50
Nasal congestion	51	61	30
Sedation	39	27	52
Increased appetite	32	21	6
Weight gain	35	20	14
Dizziness	40	35	40
Syncope	1	5	
Constipation	49	52	48
Anxiety-depression	4	3	

FIG. 19, A



Diagramatic representation of the outflow of vasoconstrictor impulses over the sympathetic nervous system to the blood vessel. The activity of this system is responsible for regulating the degree of vasoconstriction in the blood vessel and thus raising or lowering the blood pressure.

FIG. 19, B



In the patient with severe hypertension, there is a marked increase in the outflow of vasoconstrictor impulses or markedly increased responsiveness of the blood vessel to sympathetic impulses. The end result is the same resulting in severe vasoconstriction and a marked rise in blood pressure.

a very satisfactory method for treating hypertension.

The initial dose of mecamylamine, 2.5 mg. twice daily, appears to be adequate for a few patients with less severe disease. Dosage is adjusted according to the upright blood pressure. Increments in dosage are made in a "titration" fashion until the desired level of blood pressure reduction is achieved (Table 5). The drug may be given two, three or four times per day. Although there may be a cumulative effect when this agent is given at intervals shorter than eight hours, many patients, particularly those requiring large dosages, appear to have a smoother reduction with fewer untoward effects when mecamylamine is given more frequently.

TABLE 5

METHOD OF DOSE TITRATION OF MECAMYLAMINE*

	7 a.m.	*12 noon*	*5 p.m.*	*10 p.m.*
1st week	2.5 mg.		2.5 mg.	
2nd week	5 mg.		5 mg.	
3rd week	5 mg.	5 mg.	5 mg.	5 mg.
4th week	5 mg.	10 mg.	5 mg.	5 mg.
5th week	5 mg.	10 mg.	10 mg.	5 mg.
6th week	5 mg.	15 mg.	10 mg.	5 mg.
7th week	10 mg.	15 mg.	10 mg.	5 mg.

*The dose is kept constant at whatever dose on adequate reduction in blood pressure is obtained.

Peripheral or Adrenergic Blocking Agents

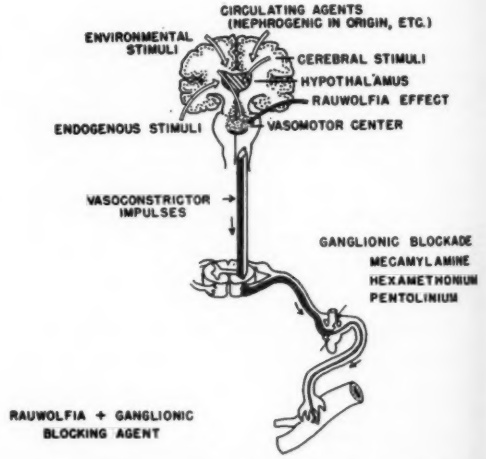
Drugs which act peripherally at the neuro-effector site are characterized by potent hypotensive activity but limited clinical usefulness because of frequent tolerance and striking untoward effects. Because these agents produce both neuro-effector and humoral blockade of vasopressor substances, there are no drugs which will combat excessive hypotension if it develops during therapy.

PHENOXYBENZAMINE (DIBENZYLINE).

Pharmacodynamics. Phenoxybenzamine blocks vasoconstrictor impulses at the neuro-effector site in the arteriole. Since sympathetic adjustment of the blood pressure to postural change is also blocked, the response is primarily an orthostatic one. Tachycardia following orthostatic blood pressure reduction is not blocked; consequently, there may be palpitation and angina during phenoxybenzamine therapy.

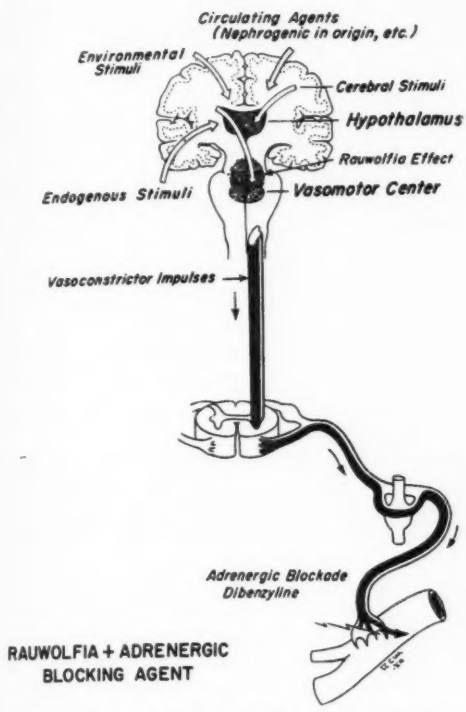
Clinical Use. Phenoxybenzamine may be

FIG. 19, C



In the patient with severe hypertension, when Rauwolfia is given, there is a significant reduction in blood pressure but the outflow of vasoconstrictor impulses remain excessive and the patient continues to be hypertensive. However, if a ganglionic blocking agent is now given in addition to the Rauwolfia, a further blockade to the outflow of vasoconstrictor impulses is established with a return of the blood pressure to normotensive levels. This is true only in the upright position and the patient may still remain hypertensive when he is supine. Also, postural reflexes are largely blocked by the ganglionic blocking agents.

FIG. 20



In the patient with severe hypertension who is given a combination of Rauwolfia and adrenergic blockade, essentially the same type of response is seen as that in figure 19, C. The Rauwolfia produces some reduction in pressure but the patient remains hypertensive. When an adrenergic blocking agent such is Dibenzyline is now added in progressively increased doses as adrenergic blockade is established, the blood pressure returns to normotensive levels. As with a ganglionic blocking agent, this is only true in the upright position and when a patient is supine, he may still have an elevation of pressure.

given either orally or parenterally. A maximum effect is obtained about two hours after oral administration. A significant reduction in upright blood pressure was obtained in 72 per cent of the patients to whom we gave phenoxybenzamine. However, side effects in all but 34 per cent of the patients prevented continuation of therapy for longer than three months. Dibenzyline in combination with Rauwolfia with or without protoveratrine,* produced a significant reduction in standing blood pressure in about 74 per cent of our patients; rendering 53 per cent normotensive. Protoveratrine appeared to add little[59] to the effectiveness of the therapy.

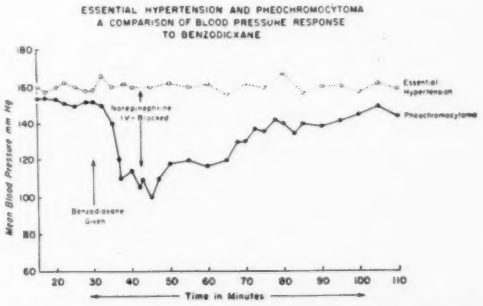
HYDERGINE. This dihydrogenated ergot preparation is effective only when given parenterally. It is probably of limited clinical usefulness because tolerance quickly develops and untoward effects are frequent.[60]

PIPEROXANE (BENZODIOXANE). This is a poor adrenergic blocking agent and is of no clinical use in treating hypertension. However, because it can block humoral pressor substances at a substantially lower dosage than is necessary for adrenergic blockade, Benzodioxane is of great clinical value as a test for pheochromocytoma (Fig. 21).

PHENTOLAMINE (REGITINE). This drug is similar to Benzodioxane and Dibenzyline. Since it blocks the neuro-effector site, the blood pressure reduction is primarily orthostatic. There is no antagonist to its use. When given orally in effective doses, nausea, vomiting, diarrhea, and weakness are common side effects. Its main value lies in its usefulness as a diagnostic test for pheochromocytoma. As with Benzodioxane, its value in the diagnosis of pheochromocytoma is dependent upon the wide range of dosage levels between that necessary for a humoral blockade of norepinephrine and the much larger amount necessary for a true adrenergic blockade.

In our experiences, less than 15 per cent of patients[59] given phentolamine orally are able to tolerate the drug for longer than one month. Although it effectively reduces blood pressure when given parenterally in adequate doses, drug tolerance develops rapidly and precludes long-term use.

FIG. 21



A comparison of the response to piperoxane, in a patient with an active pheochromocytoma by comparison to the response in another patient with essential hypertension. Piperoxane blocks circulating norepinephrine and thus sharply reduces the blood pressure in the patient with pheochromocytoma. However, this blocking agent is not potent enough to block the outflow of vasoconstrictor impulses at the neuro-effector site of the blood vessel and thus the blood pressure is not altered in the patient with essential hypertension.

*Mio-Pressin, Smith, Kline & French Laboratories, Philadelphia, Pa.

Over-all Approach to the Patient with Hypertension

All of these new potent agents should be used cautiously. Until more is learned about the pathogenesis of hypertension, treatment still consists of alleviating one symptom: the elevated blood pressure. When blood pressure reduction is achieved, it is convenient to assume that the underlying vascular disease has been stopped and that altered cerebral, cardiac, and renal physiologic processes are being reversed. This is not necessarily a true assumption. For example, the systolic hypertension of advanced arteriosclerosis is not associated with significant reversal of renal, cardiac, or cerebral damage. The elevated systolic blood pressure is merely a manifestation of altered elasticity in the arterial system. When severe hypertension is associated with deranged renal function, reduction of the blood pressure even to normal values can result in renal excretory failure. This does not mean that judicious lowering of the pressure should not be tried. The dramatic reversal of vascular changes of malignant hypertension has been reported by many authors when treatment was given before renal damage was significant. Wilkins[56] has noted that it is easier to control the blood pressure at a treatment-induced low level than to bring it down from a high level. This suggested to him that there may be some fundamental change in the underlying disease process as a result of drug therapy.

TABLE 6

OVER-ALL APPROACH TO THE HYPERTENSIVE PATIENT

Severity of Hypertension	*Initial Treatment*	*Adjunctive Treatment*[2]
Mild (Labile) Diast. 100-120 mm.Hg.	Rauwolfia[1]	
Mild (Stable) Diast. 100-120 mm.Hg.	Rauwolfia[1]	Hydralazine after 3 months[3]
Moderately severe Diast. 120-140 mm.Hg.	Rauwolfia[1]	Ganglionic blockade after 3 months[4]
Severe or rapidly progressive Diast. 140 + mm.Hg.	Rauwolfia + ganglionic[3] blockade from outset	

1. Four mg. alseroxylon (Rauwiloid), 300 mg. crude root, or 1 mg. of Reserpine per day.

2. Adjunctive therapeutic agent to be added to the regimen if the initial therapeutic agent is found to be inadequate.

3. Start on doses of 25 mg. with each meal and at bedtime increasing weekly in 25 mg. increments for each dose.

4. Start in small doses and slowly increase the dose as indicated in the discussion of each drug until the blood pressure has been lowered to the desired level in the standing position.

It is essential to establish a baseline level of blood pressures before instituting treatment. Cerebral, cardiac, and renal function should be carefully evaluated. Possible symptoms attributable to hypertension must be evaluated. The physician, on reviewing all of these factors, should determine what goals he wishes to achieve with hypotensive therapy. Although each patient requires individualized therapy, one should be able to fit all patients into a general over-all plan. The physician can avoid floundering in a series of trial and error approaches if he follows a rationale progression of therapeutic agents.

It appears desirable, at the present time, to start all patients except those with severe or rapidly progressive hypertension, on a Rauwolfia preparation alone for two to three months after control determinations are done. Evidence suggests that there is little difference in the response rate with varying available Rauwolfia preparations. This will accomplish two goals: (1) patients with mild or labile hypertension who respond to Rauwolfia alone can be spared more intensive hypotensive therapy; and (2) the Rauwolfia will block or ameliorate some of the potential untoward effects of adjunctive agents when it is necessary to use them, and will also potentiate the blood pressure response.

Rauwolfia plus hydralazine may be used in those with moderate blood pressure elevation after a suboptimal response to Rauwolfia alone, particularly in patients with significant renal damage.

Rauwolfia with ganglionic blockade by hexamethonium, pentolinium, or mecamylamine is the most potent regimen now available. It is effective in virtually all patients but may be difficult to manage without significant untoward effects. Mecamylamine, alone and in combination, appears to offer great promise. For severe and rapidly progressive hypertension, combination therapy with Rauwolfia and ganglionic blockade should be given from the outset of therapy. Combination therapy with veratrum or adrenergic blockade and Rauwolfia may be used, but these combinations seem to be associated with more untoward effects.

It is important to continue each regimen for at least several months before changing. Dosage of all drugs except Rauwolfia should be adjusted by a titration procedure. Dosage

should be determined by the upright blood pressure and care should be taken to avoid excessive hypotension, particularly when there is associated renal disease.

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SOUTHERN MEDICAL NEWS

ARKANSAS

Dr. Kenneth G. Jones and Dr. Horace R. Murphy have opened an Orthopedic Clinic in Little Rock.

Dr. and Mrs. W. J. Hunt, Magnolia, celebrated their Golden Wedding Anniversary recently. Dr. Hunt has practiced medicine for 54 years in Columbia County.

Dr. Jim McKenzie, Hope, is chief of staff of the newly opened Hempstead Memorial Hospital.

Dr. George L. Ackerman, a graduate of the University of Arkansas Medical School, has returned from a year's work in Philadelphia General Hospital and opened an office in his home town of Rison.

Dr. J. T. Irby, Earle, was honored recently by his extensive list of friends who celebrated with him his community service for 50 years. He has throughout these years been actively associated with public affairs, his church, schools and community problems.

DISTRICT OF COLUMBIA

Dr. Thomas M. Peery, professor of pathology, George Washington University School of Medicine, was named to the Executive Committee of the American Society of Clinical Pathologists at the annual meeting October 10-15 in Chicago.

Dr. Francis M. Forster, Dean of Georgetown University School of Medicine, recently accepted a special Certificate of Merit for the University from Dr. W. Ross Morris, president of the Medical Society of the District of Columbia, who presented it in behalf of the American Medical Association and Ciba Pharmaceutical Products, Inc.

Dr. Calvin T. Klopp has been elected president of the District of Columbia Division of the American Cancer Society at its ninth annual meeting held in October.

Dr. Frank E. Wilson, until recently director of the Washington office of the American Medical Association, has accepted a new appointment as executive vice-president and secretary of the Joint Blood Council, effective last November 1. Dr. Thomas H. Alphin has succeeded Dr. Wilson in the Washington office of the A. M. A.

Dr. Paul F. Dickens, professor emeritus of clinical medicine at George Washington University School of Medicine, was invited to Memphis, Tennessee recently to receive the University of Tennessee's Certificate of Merit. The award was made in recognition of Dr. Dickens' 50 years of service "to members of his community, both in the U. S. Navy and in civil life." He also received the "Golden T" from the Memphis Division Alumni Association of the University of Tennessee.

Rear Admiral H. Lamont Pugh, former Surgeon General of the Navy, assumed command of the National Naval Medical Center recently, succeeding Rear Admiral Leslie O. Stone, who has retired to enter private practice at Tyron, North Carolina.

Dr. Thomas M. Peery, professor of pathology at George Washington University School of Medicine, was invited by the University of Puerto Rico, in San Juan, to serve as Visiting Professor in Pathology the first week of November. Dr. Peery gave three lectures and conducted a clinicopathologic conference at the University.

Dr. I. Phillips Frohman was awarded a fellowship in the American Medical Writers' Association at the Association's 12th Annual Meeting in St. Louis recently. Fellowships were awarded to 19 members of the association "in recognition of high qualification, personal and professional, and of established standing as a medical writer, journalist or publisher."

Continued on page 99

EDITORIALS

CIRCULATORY DYNAMICS IN ATHEROSCLEROSIS

Atherosclerosis is thought of by pathologists as the deposit of lipid complexes including cholesterol in the aortic intima. As an important component of cardiovascular disease, our Number One Killer, atherosclerosis merits the very considerable study to which it has been subjected. The majority of these studies have had to do with metabolic and nutritional factors, age, sex, race, diets, and the like. Some interest has recently been shown in the morphology of the lesions, seeking to discover histochemical factors in the pathogenesis and pathology of the atherosclerotic lesions.

It has been known since the studies of Schultz[1] that metachromasia, now thought due to high molecular weight acid polysaccharides, increased with age in the juxtaintimal or inner part of the media. This has been noted as preceding the atherosclerosis or lipid-complex deposits in the intima. Accumulation of acid polysaccharides beneath the atheromatous plaque has been emphasized by Taylor.[2] These and other studies may have neglected the adynamic factor in the postmortem state of the aorta and other arteries.

As long ago as 1886, Thoma[3] had made paraffin casts of the aorta at blood pressure levels and found that the usual protruberant plaques are actually flattened on their surface, producing depressions and thinning in the media. As pointed out by Stewart, Birchwood, and Wells[4] in 1935, attempts to repeat this work by a number of workers were unsuccessful. However, Stewart and his co-workers, in studying a small series of hearts, seemed to have shown that atherosclerotic plaques in coronary arteries do not necessarily protrude into the lumen during life and the apparent narrowed opening seen in the dead body may not have existed during life. Harrison and Wood,[5] in 1949, injected radio-opaque material into the coronary arteries under pressure and obtained flattening of the coronary atherosclerotic plaques, producing a smooth lining for the vessels. Crawford and Levene[6] studied aortas and iliac arteries fixed in the usual way and in the distended state at arterial pressures. Noting the medial thinning overlying atheromatous plaques in the intima, they liken the process to a shallow aneurism filled by the intimal plaque.

More recently, Morgan and McManus[7] have used hydrostatic pressures to fix aortas with a manometer and a bulb of the type used for blood pressure determinations. When the aorta is filled with formalin at the systolic pressure present during life, the yellow atheromatous plaques can be observed externally to thin out and be visible through the media. According to the pressure range from zero to systolic level, the thinning of the media can be produced directly, being most marked at the highest pressure.

At a microscopic level the customary picture of the wavy internal elastic lamina is replaced in aortas fixed at physiological pressure by a thin linear arrangement of elastic tissue. The internal plaque which protrudes into the lumen of the aorta in the unfixed state can be seen to thin out the media under the normal blood pressure. In regard to the metachromatic ground substance, the accumulation of the material internal to the atherosclerotic plaque is much less in amount, or hardly increased at all when the aorta is fixed at systolic pressure.

These findings re-emphasize the necessity for an understanding and application of physiologic conditions when dynamic structures are being studied. Some hint is given also of the importance of Monckeberg's medial calcification, in which the atheromatous plaque is no longer able to thin out the hardened media. Dynamically, the aorta and other arteries have relatively fluid walls in which intima and media occupy a relative volume and together, with added materials such as atheromata, make up smooth cylinders. When underlying medial sclerosis is added, the atheromatous plaque may project further into the lumen and furnish the impedance to the circulation, with danger of eddying and thrombosis, which classical descriptions of atherosclerosis have emphasized. Similarly, reduction of blood pressure therapeutically induced, or in shock states,

may allow intramural atheroma to project into the lumen and produce obstruction. These are some of the possibilities which follow from a reconsideration of the atherosclerotic plaque as it exists during life and as it is classically described and considered. It is obvious that many ideas about vascular disease need review in terms of blood pressure.

J. F. A. McMANUS, M.D.

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QUESTIONS ABOUT COBALT THERAPY IN ANEMIA

The use of cobaltous chloride in the treatment of certain anemias had its inception after the demonstration of polycythemic effects of cobalt in animals. It has been reported that the salts of this metal are effective in certain anemias in which iron alone is usually ineffective,—in the anemias of chronic infection and of chronic renal insufficiency, and also in sickle cell anemia. It has been learned that the side effects of anorexia, nausea and vomiting can be eliminated by the use of enteric-coated tablets. Other less frequent untoward effects of cobaltous chloride have been toxic manifestations related to the eighth nerve, rash, flushing of the skin, and thrombocytosis.

Early in 1955,[1] it was reported that hypothyroidism and thyroid hyperplasia might occur as the result of cobalt therapy. Upon the observation of the development of goiter in two children being treated with cobalt, biopsies of the gland showed hyperplasia, confirmed by autopsy material from two additional patients so treated. Three children having sickle cell anemia and treated with a cobalt salt were studied from the viewpoint of thyroid function and goiter. The withdrawal of the drug permitted recovery of both clinical and laboratory abnormalities. The authors making these observations, in view of the reported effects of cobalt on several enzyme systems, postulated that cobalt had a deleterious effect on the enzymatic system in the thyroid gland in which inorganic iodide is oxidized, bound, and converted to thyroxin. At their suggestion Kirkwood studied the effect of cobalt on the tyrosine iodinase system and found that it inhibits this enzyme system.

Other studies have been reported as the result of this report. Klinck[2] reported that of ten instances of thyroid hyperplasia, studied in the preceding two years at the Armed Forces Institute of Pathology, leading to interference with breathing or to death by suffocation, five had received cobalt and iron therapy. The pathologic picture in those having had the drugs and those who had not was indistinguishable.

Holly[3] reported upon the use of cobaltous chloride and iron in combination, cobalt alone, and iron alone in pregnant women with a control of normal pregnant women. He found that though the combination cobalt and iron prevented reduction in the mean hemoglobin level and hematocrit during pregnancy, neither they nor those receiving cobalt alone, showed enlargement of the thyroid gland nor were any abnormalities observed in the offspring. Jaimet and Thode[4] in observing the effect of a cobalt-iron preparation upon thyroid function after five and again ten weeks of administration in children were unable to demonstrate any depression of function nor goiter. Scott and Reilly[5] in studies on rats suffering from transmissable fibrosarcoma found that after 44 days of treatment with cobalt no abnormality of function of the thyroid gland was demonstrated though polycythemia was marked and there was significant retardation of growth of the fibrosarcoma.

In view of this discussion of the possible deleterious effect of cobalt on thyroid function an evaluation of its place in the treatment of anemia is to the point. The opinions of several hematologists[6] who expressed themselves on this question are therefore of interest. Though cobalt may be effective in the hitherto refractive anemia of uremia, chronic infection, and malignancy, it may do so through the disturbance of normal physiologic processes which may in itself have far-

reaching implications. The evidence suggests that cobalt interferes with intracellular transport of oxygen. In animals cobalt induces polycythemia. Its effect on human anemia seems thus to be the same mechanism which may lead to polycythemia developing at high altitudes,—the result of relative anoxia. In some way this tissue anoxia is a greater stimulus to the bone marrow than the as yet unknown pathologic effect of chronic inflammation and uremia on erythropoiesis. In other words, it seems that in obtaining a hematologic response to cobalt therapy, one may be producing a state of disease to provoke such a response.

If the creation of an abnormality for an erythropoietic effect were the only one, the end result might be justified. But before the clinician can blindly accept this, he must consider other important enzyme systems involving tissue oxidation, as in the case of the tyrosine iodinase system already mentioned. Angina pectoris and claudication of leg muscles have been reported in the course of cobalt therapy, probably further evidence of hypoxia.

Nor do the studies alluded to previously, which failed to substantiate thyroid hyperplasia, disprove the observations of Kriss and associates.[1] The negative studies relate to normal pregnant women and children. The hyperplasia was reported in persons who were ill. It is conceivable that the blocking of enzyme systems in a normal person may be of such degree that the usual biologic factor of safety prevents anything but a subclinical manifestation of dysfunction, whereas in an organism already disturbed a physiologic abnormality may produce an untoward effect. Clinical experience is replete with such examples.

From such thinking and the opinions of hematologists, it would seem that the average physician had better use his iron therapy, so effective alone in iron deficiency anemias, "unpotentiated" by cobalt until more is known concerning the effects of this potent metal in the tissue economy.

EDITOR.

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2. Klinck, G. H.: Thyroid Hyperplasia in Young Children, J.A.M.A. 158:1347, 1955.
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OF INTEREST TO YOUNG PHYSICIANS OF THE SOUTH

The Council and Officers of the Southern Medical Association have taken steps which will be of interest to the young doctors of the South.

In its desire to further the continued education of the doctor after graduation, the Southern Medical Journal will be available to internes and residents at three dollars per year. By this reduced subscription rate the Association is making a large contribution to postgraduate education. Becoming acquainted with the Southern Medical Association through the Journal, the future practitioner of the South will see in later membership in the Association its contribution to his continuing education in the years ahead.

Another interesting development will be the invitation of a representative of the fourth year class of certain medical schools, within a given radius of the annual meeting place, to attend the meeting with expenses paid.

These two moves by the Council and Officers should bear fruit in an acquaintance of the younger generation of doctors with the Southern Medical Association. They will learn of its great function in continuation education of the doctor after graduation. And through this they will build good fellowship at the annual session in meeting classmates and the former associates of their house-staff years.

These are forward looking steps for the good of the Association.

EDITOR.

THE NEW GOLD COVER

Of course, you *had* noticed the gold cover on this Journal! But why would a sedate and discreet publication like a medical journal come out with such evidence of opulence? Could it be that the coffers of the Association are running over, and that *your* money cannot be put to better use?

No, it's not affluence—it's not a typographer's trick! The gold cover which will adorn every issue of the Journal for 1956 has a very special purpose. It is simply another way to tell 10,700 physicians that 1956 is the GOLDEN ANNIVERSARY OF THE SOUTHERN MEDICAL ASSOCIATION!

The color of the cover, symbolizing fifty years of history, has a very special significance. It connotes a major milestone in the life of an organization which has played a strategic role in medical progress, not only in the South, but within the nation and beyond its borders. It represents the organized medium through which stalwarts of medicine have wielded a profound influence upon their confreres with the result that tens of thousands of doctors have practiced better medicine.

Then, too, it may be hoped that this gold cover may also be prophetic—a token of a golden future for a unique medical organization.

Yes, we're proud of the right—the propriety—of using a gold cover for a full twelve months. We're proud of the past, we're appreciative of the present, and we're hopeful for the future.

V. O. FOSTER

THE HOUSTON MEETING

In retrospect, and from an administrative point of view, the 49th Annual Meeting of the Southern Medical Association was a good meeting. Held in Houston on November 14-17, with more than five thousand persons in attendance—physicians, ladies, exhibitors, medical students, interns, residents, nurses, visitors and others—the meeting meant a lot of things to a lot of people. Broadly, there were three major areas of interests and activities in which a multitude of events contributed materially to the coordinated whole—always referred to as "the meeting." These areas were EDUCATION, BUSINESS, PLEASURE. (See photographic montage of meeting on pages 90 and 91).

Postgraduate Education Features

A broad scientific program, constituting the Scientific Assembly of the Association, was well attended by physicians. The Assembly formally consists of the regularly scheduled sessions of the 20 organized Sections of the Association. These Sections which represent the major medical and surgical specialties and general practice are: Allergy, Anesthesiology, Dermatology and Syphilology, Gastroenterology, General Practice, Gynecology, Industrial Medicine and Surgery, Medicine, Neurology and Psychiatry, Obstetrics, Ophthalmology and Otolaryngology, Orthopedic and Traumatic Surgery, Pathology, Pediatrics, Physical Medicine and Rehabilitation, Proctology, Public Health, Radiology, Surgery, and Urology.

The above Sections held a total of 51 one-half day sessions with 50 to 300 physicians in attendance at each session. Each Section, with its own officers, planned and presented its scientific program. The regular sessions were supplemented with joint sessions of related specialties, panels, symposia, and clinical sessions in various Houston hospitals and other medical facilities.

Special Program in Geriatrics

The Houston meeting, for the first time, presented a formal Symposium in Geriatrics. Moderated by Dr. A. Clayton McCarty, Louisville, Kentucky, and planned jointly by Dr. McCarty and Dr. Milford O. Rouse, Dallas, Texas, it presented eight prominent panelists who discussed the major medical and surgical problems of the "older age group." The symposium was keynoted by Dr. Edward Henderson, Montclair, New Jersey, president of the American Geriatrics Society.

Conjoint Societies

Further specialized papers were presented during the scientific sessions of the following societies which met conjointly with the As-

HOUSTO SHL

(1) President R. L. Sanders delivers presidential address (2) Dr. Francis P. Gaines addresses opening assembly (3) Presentation of George D. Feldner Doctor's Day Trophy to Bradley County, Tennessee Auxiliary (4) Typical Texas welcome (5) Speaker's Table—Opening Assembly (6) Registration

USTO GHLIGHTS

(7) Meeting of Council and Section Officers (8) Annual dinner followed by (9) Dance (10) Presentation of Past President's Medal to Dr. Sanders by Dr. M. O. Rouse, Chairman of Council (11) Mr. C. P. Loranz receives first Golden Anniversary Key from Dr. Rouse. (12) Dr. Sanders presents gavel to incoming President W. Raymond McKenzie

sociation: American College of Chest Physicians, Southern Chapter; Association for Research in Ophthalmology, Southern Section; Southern Gynecological and Obstetrical Society; College of American Pathologists, Southeastern and South Central Regional Committees; Southern Society of Cancer Cytology, and the Women Physicians of the Southern Medical Association.

Exhibits

A capacity number of both scientific and technical exhibits further broadened the teaching program of the meeting. The limited facilities of the exhibit hall required not accepting many fine exhibitors, both from consideration of floor space and the Association's policy of maintaining a balance between the scientific (physician) and technical (commercial) exhibits. Fifty-five physician's exhibits and 83 technical displays added much to the physician's armamentarium of medical and surgical therapeutics and technics.

Tours of the Texas Medical Center

Finally, from the educational standpoint, more than 500 physicians took advantage of regularly conducted tours of the fabulous Texas Medical Center and other Houston medical facilities.

Business

While the nature of the Southern Medical Association, dedicated only to the advancement of medicine, precludes business considerations of the social, economic, and political aspects of the practice of medicine, hundreds of man-hours were unselfishly invested in the business side of the Association's affairs in Houston. The Council, a seventeen-member body, met in three full-dress sessions. Being the basic and only policy-making body of the Association, its decisions govern the activities, programs, and projects undertaken by the Association. Prior to the Council sessions, the Executive Committee composed of six members met for the purpose of reviewing reports of officers and committees, and drafting recommendations for the Council's consideration.

Council Action Highlights

Among the major actions taken by the Council were the following:

1. Heard and accepted reports from the Executive Secretary-Treasurer, the Business Manager, the Advisor and Professional Relations Counselor, the Editor of the Journal, and the President of the Woman's Auxiliary.

2. Adopted the budget for the next fiscal year.

3. Recommended adoption of certain amendments to the Constitution and By-Laws to the two general sessions of the membership (recommendations adopted by general sessions).

4. Established the following schedule of meeting places: Miami Beach, 1957; New Orleans, 1958; Atlanta, 1959; and Baltimore, 1960. (1956 Meeting—Washington, D. C.)

5. Reaffirmed its position of not accepting Journal advertising involving alcoholic beverages.

6. Directed an additional contribution to the Association's Retirement Fund.

7. Created a Distinguished Service Award and provided for its operation.

8. Directed that proper ceremonies be held in Chattanooga, Tennessee, on October 2 and 3, 1956, commemorating the founding of the Association there in 1906.

9. Provided for the compiling of a history of the Association in connection with the Chattanooga observance and the Golden Anniversary Meeting in Washington, November 12-15, 1956.

10. Determined the general over-all plan of the 1956 Golden Anniversary Meeting.

11. Established a special subsidized Journal subscription rate for interns and residents in the South.

12. Authorized and directed the appointment of the following committees, among others:

a. Committee to explore possibilities for a permanent home (headquarters) for the Association
b. Committee on medical student representatives to the annual meetings
c. Committee on expenses of guest speakers
d. Committee on life membership.

Other Business Sessions

In addition to the deliberations of the Council and the Executive Committee, business sessions of the following operating

agencies were held: Editorial Board, Joint Session of the Council and Section Officers, and business sessions of the 20 Sections, including the election of Section Officers.

General Business Sessions of the Membership

Two general sessions of the membership, held on Monday morning, November 14, and Wednesday evening, November 17, were attended by record numbers in recent years. The Monday morning meeting featured the presidential address by Dr. R. L. Sanders of Memphis, and an address by Dr. Francis Pendleton Gaines, President of Washington and Lee University. Dr. Gaines was the President's special guest for the Houston Meeting.

The Wednesday evening affair, held in the Emerald Room of the Shamrock, featured the Annual Dinner, a brief business session and the Annual Dance.

Officers elected at this session by the membership were:

President-Elect, J. P. Culpepper, Jr., Hattiesburg, Mississippi.

First Vice-President, W. Kelly West, Oklahoma City, Oklahoma.

Second Vice-President, Denton Kerr, Houston, Texas.

Officers elected by the Council were as follows:

Chairman of the Council, J. Morris Reese, Baltimore, Maryland.

Vice-Chairman of the Council, A. Clayton McCarty, Louisville, Kentucky.

Member, Executive Committee, Henry H. Turner, Oklahoma City, Oklahoma.

Member, Board of Trustees, R. L. Sanders, Memphis, Tennessee.

Other highlights of this session featured the installation of the incoming President, W. Raymond McKenzie, Baltimore; the presentation of the Past President's Medal to R. L. Sanders of Memphis; and the presentation of a special "Golden Anniversary Key" to Mr. C. P. Loranz, Birmingham, the Association's Advisor and Professional Relations Counselor, in recognition of his 43 years of loyal and efficient service.

The evening was concluded with the Annual Dance and professional entertainment with a capacity audience.

Woman's Auxiliary

The Woman's Auxiliary to the Southern Medical Association held its 31st Annual Meeting in Houston during the meeting of the Association. Its meetings, presided over by its President, Mrs. Louis K. Hundley of Pine Bluff, Arkansas, was attended by more than 1,000 registrants—three times the Auxiliary's usual registration. Mrs. John J. O'Connell of St. Louis was installed as President of the Auxiliary and will preside over its 32nd Annual Sessions in Washington, D. C., November 12-15, 1956. This meeting will be held during the same time as the Association's "Golden Anniversary" meeting in the nation's capital over which President W. Raymond McKenzie of Baltimore will preside.

Social Affairs

The Southern Medical Association, noted for its friendship and a distinctive spirit of confraternity, was honored by having 19 medical school alumni and medical fraternity groups hold reunions and other social functions during the Houston meeting. Section luncheons and dinners, together with the delightful social affairs of the Auxiliary and other groups such as the "Southern Flying Physicians"—all added much to the pleasure and spice of an excellent scientific menu.

Our Thanks

The Texas Medical Association, the Harris County Medical Society and its Auxiliary, and an effective and cooperative Local Committee on Arrangements chairmanned by Dr. Denton Kerr seemed to have eclipsed all previous evidence of a genuine hospitality—constituting a particular kind of welcome which only TEXANS can extend. Yes, it was a good meeting!

V. O. Foster

25 YEARS AGO

Addison's Disease*

"In the last twenty years, 115 cases of Addison's disease have been observed in the Mayo Clinic. In the early days there was no specific plan of treatment, and the results were almost always uniformly bad. Prior to 1920, desultory efforts at substitution therapy were made, with occasional success. Since then every patient with Addison's disease who has gone to the Mayo Clinic has been given special consideration from the standpoint of substitution therapy, and considerable progress has been made. . . .

"The natural course of the disease is usually progressively downward, with acute exacerbations at irregular intervals. Spontaneous remissions, persisting for a number of weeks, months or even years, may occur, and an occasional patient seems to recover spontaneously.

"Several factors must be taken into consideration in the treatment of patients with Addison's disease: (1) the nature of the underlying disease and its treatment; (2) the natural course of the disease; (3) the general care of the patients; (4) the treatment of symptoms and complications, and (5) the results of specific organotherapy.

"Good general treatment includes abundant rest, warmth, relaxation, freedom from work and worry, protection against stresses and strains of all kinds, and an adequate intake of food and fluids. Mention should be made of the tremendous value of a solution of dextrose, 10 per cent, and sodium chloride, 1 per cent, administered intravenously in the crises and terminal stages of the disease; these events are attended by marked dehydration. . . .

"Organotherapy is as old as the disease. . . .

"In presenting our results in the treatment of Addisons' disease, we wish to recall the restraint and conservatism that characterized Addison's original description. We hope that in so doing we will avoid "hasty pretentions," "partial and prejudicial observations" and "overstatements of facts," which, according to Addison, should "merit the just rebuke of those possessing sounder or more dispassionate judgment."

"In 1920, a regimen was instituted in the case of the late Dr. Muirhead, who was suffering from Addison's disease. It was decided to utilize epinephrine to the point of tolerance, administering it subcutaneously, by rectum and by mouth repeatedly during the day, and in the maximal dose which could be tolerated by each channel of administration. In addition, whole suprarenal substance of suprarenal cortex was administered by mouth.

"The immediate results in Dr. Muirhead's case were remarkable. Whereas he had been bedridden on arrival, he left for home within a few weeks, feeling well on the way to recovery. He lived less than a year, however. Since that time 57 patients who have gone to the Mayo Clinic with Addison's disease have been subjected to the Muirhead treatment. Thirty-two cases are reported as temporarily benefited, and in 20 of these the immediate results were excellent. In some cases this period of improvement lasted for weeks, in others for months, and in ten cases for periods of from three to seven years. In contrast to this, the treatment was entirely without beneficial effect in 25 cases. . . .

"Numerous investigators have attempted for many years to isolate a cortical hormone for the treatment of Addison's disease. Among these were Rogoff and Stewart, Hartman and his collaborators, Roehler, and Swingle and Pfiffner. Increase in the time of survival of animals following bilateral suprarenalectomy had been set up as the criterion of efficacy of these preparations. . . .

"The preparation of an aqueous extract of the suprarenal cortex which would maintain indefinitely the life of bilaterally suprarenalectomized cats was announced by Swingle and Pfiffner in March, 1930. Subsequently they reported that by the administration of this extract they were able to revive comatose animals that were prostrate and on the verge of death from suprarenal insufficiency, and also to restore them to an apparently normal condition and to keep them in a semblance of perfect health by daily injections.

"The significance of such an announcement and the interest aroused by the possibility of using this extract in clinical medicine are obvious. An extensive experience with the so-called Muirhead treatment in cases of Addison's disease convinced Rowntree and Greene of the futility of ordinary therapeutic measures in combatting the crises of acute suprarenal insufficiency. . . . This point was further emphasized May 31, when the patient whose case is reported in Case 1 was admitted to the hospital in collapse. The outlook seemed hopeless, but as a last resort a telegram was sent to Swingle and Pfiffner and they forwarded a supply of their cortical hormone by air mail. Since that time, it has been possible to observe the effect of this preparation on six additional patients suffering from Addison's disease. The amount of cortical hormone available for clinical use has been small and its delivery irregular, so that as yet it has not been possible to make a complete clinical study. The results to date, however, warrant this preliminary report. . . .

"The results in these cases convince us of the efficacy of this cortical hormone. The disappearance of anorexia, the increase of appetite to the point of hunger, the gain in weight, and the definite euphoria were striking in all cases. As long as the preparation could be administered, the results were all that could be desired. . . . The immediate results in a crisis are excellent. The disease, however, is chronic, and it will be necessary for several years to elapse before a final appraisal can be made of the

*Rowntree, Leonard G., Greene, Carl H., Swingle, Wilbur W., and Pfiffner, J. J.: Addison's Disease, Experiences in Treatment with Various Suprarenal Preparations, J.A.M.A. 96:231, 1931.

value of this cortical hormone in Addison's disease. The first three patients had previously been under the Muirhead treatment and all three stated that they felt better when this cortical hormone was given than with any treatment which they had received before. . . .

"In five instances, in the face of a crisis or of an impending crisis, the administration of but 40 to 60 cc. of the hormone we are using, in divided doses, over several days, has at least temporarily restored the patients to apparent health, within a period of from two to five days. The effects last for a period of from one to three weeks. The peak of the improvement is manifest in about a week subsequent to administration, and this is followed by general decline, with active symptoms reappearing in a period of from 10 to 14 days.

"The return of appetite and the increase in weight have been the most striking that we have witnessed in our entire experience with this disease. We are inclined to believe that the cortical hormone is as effective in meeting the crisis of Addison's disease as is insulin in diabetic coma. Although somewhat less prompt and dramatic in action, the results are almost equally striking. Danger lurks in every exacerbation. In the cortical hormone we apparently have a reliable remedy. With unlimited supply of the hormone, it is possible that patients may be completely rehabilitated. This, however, is a matter yet to be determined."

DOCTOR—Don't Overpay Your Taxes*

WHETHER the federal income tax rates are cut or not, you may be able to cut your own tax bill—honestly!

To do this you need to know the tax effect of various choices. Your choice of a method of handling a particular transaction can raise or lower your taxes, and sometimes you can save money by a legitimate shift of taxable income or deductions from one year to another. You are also allowed choices in your treatment of certain items in your tax return, such as depreciation and research costs.

Many businesses and professional people could reduce their tax burden if they were aware of the tax considerations affecting a variety of transactions. The most feasible means for many businesses to keep alert to tax saving opportunities is frequent consultation with a properly qualified advisor. If the firm retains a certified public accountant or a firm of CPAs, there should be tax consultations not just once a year when the filing date approaches, but throughout the year as decisions are made which will affect the tax.

Choice of Depreciation Method

Certain tax-saving steps are still possible at tax-filing time. One of them is the proper choice of depreciation method. The first step is to determine the estimated useful life of any asset acquired during the tax year. Every businessman should have a copy of "Bulletin F," which contains tables of "average" useful lives. It is available from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., for 30 cents. The tables provide a guide, but it is not necessary to follow them exactly.

The simplest method is straight-line depreciation. It may also be the best in your particular case. Just divide the cost (less what you expect to sell it or trade it in for when it is replaced) by the number of years of estimated useful life, and this is the amount to be deducted each year. In arriving at the original cost, don't forget to include freight and installation charges in addition to the price paid for the equipment.

The law now specifically permits several other methods of depreciation for new assets having a useful life of three years or more. One of them is known as the declining balance method. In the first year the depreciation rate is twice what it would be under the straight-line method. The next year the same rate is applied to the amount remaining to be depreciated. This process is repeated each year.

The result is that a greater proportion of the cost is depreciated during the early years of the life of the asset.

*This article is based on information supplied by the American Institute of Accountants, the national professional organization of certified public accountants.

Another new method, known as "sum of the years' digits," has a similar effect. You should figure depreciation on a new asset in all possible ways so that you can decide which is best for you and make the proper choice.

These methods of rapid depreciation may be particularly helpful to a company which is currently making large outlays for new equipment, but the depreciation left for the later years of the asset's life will be less than under the straight-line method. The best method depends upon the circumstances of the individual company, and is also affected by such imponderables as estimates of future earnings and tax rates during the life of the asset.

Research and Development

Another choice confronting the taxpayer is whether to treat research and development costs as immediately deductible expenses or to amortize them over a period of years. The immediate deduction is certainly a "bird in the hand" and may be very attractive to a physician who needs this tax benefit to help finance the undertaking.

The taxpayer who can afford to spread the cost over the estimated useful life (or at least sixty months if the useful life cannot be determined) may find it best to do so. This is especially likely to be advantageous for those whose income is expected to increase.

Being Taxed as a Corporation

There is a provision in the 1954 Internal Revenue Code which allows some proprietorships and partnerships to be taxed as if they were corporations. This choice should not be made lightly, as there is considerable uncertainty about the provision and the proprietorship or partnership desiring corporate tax treatment might find it better actually to incorporate.

Choice of Fiscal Year

Regulations now permit changes of fiscal year in some cases without permission of the Treasury Department. Generally it is wise to use the fiscal year which corresponds most nearly with the annual cycle of business operations, ending at the low point of receivables, inventories and loans, instead of a calendar year. This reduces the area of possible dispute over such matters as value of inventories, and has many advantages apart from tax considerations. The change should be carefully timed, though, to avoid possible adverse tax effects during the change-over period.

Sickness and Accidents Benefits

Under the present tax law, payments from your company employees for treatment of sickness or injury are not taxed as income of the employees. If the company has a plan for continuing all or part of an employee's pay while he is absent for sickness or injury, limited amounts of this "sick pay" are also tax exempt.

This applies whether the payments are made by the company or by an insurance company. In the case of a sickness requiring hospitalization even for one day during the course of the illness, or in the case of *any* injury, the first $100 per week of payments are tax free. In the case of sickness which does not require as much as a day's hospitalization, the exemption begins after the first week of absence.

No great formality is required concerning the "plan" but it should be explained to employees, and appropriate records kept of the amounts paid. Proposed regulations governing tax withholding in 1956 from payments to ill employees were still under discussion when this article was prepared.

Repairs and Improvements

If you contract for repairs and improvements to your business property, be sure that these two types of work are billed separately. Should you lump them together, you may find that the entire cost has to be capitalized for future depreciation. By listing the cost of repairs as a separate item you are allowed to deduct it as an expense of the current year.

For example, you might have a furnace repaired and new radiators added. By separating the charges you can deduct the cost of the repairs in the current year, although the new radiators would be improvements subject to depreciation during their useful life.

Keeping Good Records

Many deductions are lost through failure to keep adequate business records. Be sure

that you have good records to show you what deductible expenses you have had, and to back up your deductions in case they are questioned by the Government. This applies particularly to your out-of-pocket business expenses, such as travel and entertainment of customers, and to items which are deductible on your personal income tax return.

Good records and properly qualified professional tax assistance—at tax-filing time and throughout the year—are the keys to income tax savings.

BOOK REVIEWS

Applied Medical Bibliography

By William Dosite Postell, Medical Librarian and Professor of Medical Bibliography, Louisiana State University School of Medicine. American Lecture Series. 142 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price: $4.50.

The author states the purpose of the book is to present to the medical student an outline of the arrangement and organization of the medical library, to present to him the basic reference tools of a medical school library, and provide an appreciation of bibliographic methods.

The first section deals with historical bibliography, and includes a discussion of the manuscript, the medical book and medical societies, and the medical journal. In Part II, the author discusses modern bibliography, including basic reference books, indexes, and the periodical collection. The third section deals with the scientific paper, including instructions in preparation. There is also a chapter on documentation.

Three appendixes follow, including a section on "Study Questions."

The historical sections and those dealing with library organization are the best. The section on basic reference books and periodicals leaves much to be desired. Perhaps the most serious fault is that it presents medical literature in such a way that the student, because of the emphasis on works in the English language, fails to get a concept of medicine as a world literature. Search failed to reveal mention of any of even the most important foreign reference works or journals although such items are to be found in most of the medical school collections in this country. These shortcomings mean that the book fails to give the medical student the kind of introduction to the literature of his field that has been so ably provided for the chemistry student by such works as Soule's *Library Guide for the Chemist*, Dyson's *Short Guide to Chemical Literature*, and Mellon's book on *Chemical Publications*.

The grouping of material seems at times illogical from the point of view of use. For example, in the section on dictionaries the extremely useful modern polyglot dictionaries are discussed and grouped under "bilingual" dictionaries, a misleading characterization.

In the discussion of source material for drugs, so important to the modern student, such a useful tool for this purpose as *New and Non-Official Remedies* is discussed under the category of "Medical Yearbooks," and *Unlisted Drugs* is not mentioned at all. The section on "Medical Yearbooks" is misleading because it fails to link this category with such important medical yearbooks as, for example, the *Annual Review of Medicine* and the series of *Year Books*, which include Medicine, Surgery, Pediatrics, etc., which are discussed elsewhere under "Review Journals."

The section on biographic reference works gives practically no information regarding the international and foreign biographical directories. The lack of accurate bibliographic information at the point where titles are listed forces the reader to search the text where it is sometimes, but not always, mentioned.

Perhaps the most astonishing omission in this chapter is the failure to refer the student to the Medical Library Association's *Handbook of Medical Library Practice*, (2nd edition in press), which has an extensive list, arranged by subject comprising almost two thousand of the most important reference works in medicine and constituting an invaluable source book for anyone wishing to become familiar with medical reference books.

The typography of the specimen pages reproduced from other works is very poor, the print having been reduced so much in some instances that it is practically illegible. The index is inadequate for a book of this type.

Experimental Pharmacodynamics

By T. Koppanyi and A. G. Karczmar. 256 pages. Minneapolis, Minnesota: Burgess Publishing Co., 1955.

This book is a laboratory manual of pharmacology or pharmacodynamics, which outlines in detail, experiments for the study of the effect of drugs on the living organisms with particular reference to man. In addition to the outline of the laboratory procedure, a discussion of the importance of the experiment is also presented with frequent references to background material including mechanism of drug action. This monograph can be recommended highly as a laboratory manual for students in pharmacology. It is one of the most comprehensive and best written manuals on this subject. It is particularly valuable for those working with experimental animals as it includes the dosage of drugs for a variety of experimental animals. Such information is difficult to obtain, and has not recently been published in any other compact unit.

BOOKS RECEIVED

Atlas of Rush Pin Technics. A System of Fracture Treatment. By Leslie V. Rush, M.D., F.A.C.S., F.I.C.S., Department of Surgery, Rush Memorial Hospital, Meridian, Mississippi. 227 pages, illustrated. Meridian, Mississippi: The Berivon Company, 1955.

Planning Florida's Health Leadership. Medical Education in the University. Edited by Louis J. Maloof, A.B., 1949; M.A., 1950, University of Georgia, Athens, Volume 5. 161 pages. Gainesville, Florida: University of Florida Press, 1955. Price $1.50. (Communications relating to the Medical Center Study Series should be addressed to Dr. Russell S. Poor, Provost, The J. Hillis Miller Health Center, University of Florida, Gainesville.)

The American Academy of Orthopaedic Surgeons Instructional Course Lectures. Edited by R. Beverly Raney, M.D., Chapel Hill, North Carolina. Volume XII. 287 pages, illustrated. Ann Arbor, Michigan: J. W. Edwards, Publisher, Inc., 1955. Price $10.75.

Infant Nutrition in the Subtropics and Tropics. By D. B. Jelliffe, M.D., M.R.C.P., D.C.H., D.T.M. & H. World Health Organization Visiting Professor of Paediatrics, All-India Institute of Hygiene and Public Health, Calcutta. 229 pages. New York: Columbia University Press, 1955. Price $5.00.

Dried BCG Vaccine. By Yoji Obavashi, M.D., Assistant Chief, Research Department, Research Institute, Japan Anti-Tuberculosis Association, Tokyo, Japan. 214 pages. World Health Organization. New York: Columbia University Press, 1955. Price $5.00.

Group Processes. Transactions of the First Conference. Edited by Bertram Schaffner, M.D., Columbia University. 317 pages. New York: Josiah Macy, Jr. Foundation, 1954. Price $5.50.

Pathology Seminars. Edited by Robert S. Haukohl, M.C., Assistant Professor of Pathology, Marquette University School of Medicine, Milwaukee, Wisconsin; and W. A. D. Anderson, M.D., Professor of Pathology and Chairman of the Department of Pathology, University of Miami School of Medicine. 191 pages. St. Louis: The C. V. Mosby Company, 1955. Price $10.00.

New Concepts in Surgery of the Vascular System. By Emile Holman, M. D., Professor of Surgery, Stanford University School of Medicine, San Francisco. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $3.50.

Community Programs for Mental Health. Edited by Ruth Kotinsky and Helen L. Witmer. 358 pages. Cambridge, Mass.: Published for the Commonwealth Fund by Harvard University Press, 1955. Price $5.00.

Clinical Analgetics. By E. G. Gross, M.D., Professor and Head of Department of Pharmacology, State University of Iowa, College of Medicine, and M. J. Schiffrin, Ph.D., Assistant Director of Clinical Research, Hoffman-LaRoche, Inc., Nutley, New Jersey. 91 pages, American Lecture Series. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $3.00.

A Textbook of Clinical Pathology. Edited by Seward E. Miller, M.D., Medical Director United States Public Health Service; Chief, Division of Special Health Services, Washington. Fifth Edition. 1115 pages, illlustrated. Baltimore: The Williams and Wilkins Company, 1955. Price $11.00.

Problems in Amoebiasis. By Charles William Rees, Ph.D., Head, Section on Protozoal Diseases, Laboratory of Tropical Diseases, National Microbiological Institute, National Institutes of Health, Bethesda, Maryland. 109 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $4.75.

The Back and Its Disk Syndromes. By Philip Lewin, M.D., Professor Emeritus and Formerly Chairman of Orthopedic Surgery, Northwestern University Medical School; Professor of Orthopedic Surgery, Cook County Graduate School of Medicine, Chicago. 920 pages, 371 figures and 4 color plates. Second Edition, thoroughly revised. Philadelphia: Lea and Febiger, 1955. Price $18.50.

The Pediatric Years. By Louis Spekter, M.D., Director, Bureau of Maternal and Child Hygiene, Connecticut State Department of Health. 709 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $12.50.

Obstetrical Anesthesia. By Bert B. Hershenson, M.D., Director of Anesthesia, Boston Lying-In Hospital, Clinical Associate in Anesthesia, Harvard Medical School. 375 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $9.50.

Proceedings of the Third Medical Conference of the Muscular Dystrophy Associations of America, Inc. 324 pages. New York, 1954.

Chronicle of the World Health Organization. Vol. 9, No. 9. New York; Columbia University Press, 1955. Price $0.30.

Hypothermic Anesthesia. By Robert W. Virtue, M.D., Associate Professor and Head of Division of Anesthesiology, University of Colorado School of Medicine, Denver, Colorado. American Lecture Series. 62 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $2.50.

Classics of Biology. By August Pi Suner, English translation by Charles M. Stern. 323 pages. New York: Philosophical Library, 1955. Price $7.50.

The Relief of Symptoms. By Walter Modell, M.D., Associate Professor, Clinical Pharmacology, Cornell University Medical College. 427 pages. Philadelphia: The W. B. Saunders Company, 1955. Price $8.00.

How to Reduce Surely and Safely. By Herbert Pollack, M.D. with Arthur D. Morse. 152 pages. New York: McGraw-Hill Book Company, Inc. 1955. Price $2.95.

District Nursing. By Eleanor Jeanette Merry, S.R.N., and Iris Dundas Irven, S.R.N. Queen's Institute of District Nursing. 251 pages. Second Edition. Baltimore: Williams and Wilkins Co., 1955. Price $4.50.

SOUTHERN MEDICAL NEWS

Continued from page 85

Dr. Harvey Ammerman and Dr. Laszlo Ormandy were elected to fellowship in the International College of Surgeons during the recent meeting of the U. S. Chapter in Philadelphia.

Dr. Reamur Donnally has been named Advisory Editor on Medicine for the Encyclopedia Americana. He will help prepare articles in the field of medicine, advise the editorial staff in selecting contributors for medical subjects, and write some medical articles.

Dr. Carlton N. Price has returned from a six weeks' tour of the Far East, an assignment he carried out for the Surgeon General of the Army. Dr. Price visited all the American base hospitals in Japan, Korea, Okinawa, and Honolulu.

Dr. Samuel M. Dodek, associate clinical professor of obstetrics and gynecology, George Washington University School of Medicine, attended the 14th British Congress of Obstetrics and Gynecology in Oxford, England, and participated in a symposium on "The Management of the Unhealthy Cervix."

Dr. George Maksin, chairman of the Committee on Public Information of the District of Columbia Medical Society, was named by the District Commissioners to a seven-member Board of Appeals and Review to hear cases under the city's newly adopted Housing Code.

Dr. Robert E. Moran was appointed chairman of the Rehabilitation Committee of the American Society of Plastic and Reconstructive Surgery at the recent annual meeting of the society.

Dr. Charles P. Cake, director of the Division of Tuberculosis Control for Arlington County, Virginia, was elected president of the Southern Tuberculosis Conference at the conclusion of a three-day meeting in Louisville, Kentucky recently. Dr. Cake is an associate member of the District Medical Society.

Dr. Bela Gondos, Washington radiologist, has been

appointed chief of the Department of Radiology of the District of Columbia General Hospital.

Dr. Peter D. Comanduras, a member of the board of trustees of the District of Columbia Division of the American Cancer Society, was one of the judges for a school essay project in the District of Columbia. The topic for the essay is "Youth Looks at Cancer" and is open for competition to students in the tenth, eleventh and twelfth grades.

Dr. George I. Mishtowt left recently for Baghdad, Iraq, to be gone about two years. In Baghdad he will be a member of the American Embassy as medical attaché to the Middle East.

Dr. Peter N. Lombard, an affiliate member of the District Medical Society, has been elected to the Board of Directors of the Kiwanis Club of Silver Spring.

Dr. Karl H. Wood is an associate member of the District Building and Loan Association. He succeeds his father, the late Dr. Harold A. Wood, who served on the board since 1934.

FLORIDA

Dr. Gretchen V. Squires, Pensacola, chairman of the medical division of the local Community Chest, recently presented the Pensacola Community Chest a check for $7,250 in the annual Red Feather campaign on behalf of the Escambia County Medical Society. This represents the largest gift in the history of the medical division of the local Community Chest. Dr. Squires is vice-chairman of the Section on Pathology of the Southern Medical Association.

Dr. G. Dekle Taylor, Jacksonville, has been appointed a member of the Duval County Welfare Board.

Dr. James J. DeVito, St. Augustine, has returned from Boston where he took a postgraduate course at the Harvard University Medical School.

Dr. Barney Weinkle, Miami Beach, has been honored by the city employees there for "his courtesies and his services beyond the call of duty." Dr. Weinkle was presented a plaque as tribute.

Dr. Walter C. Payne, Sr., Pensacola, has been reappointed by Governor LeRoy Collins to the Advisory Hospital Council for the state of Florida. Dr. Payne also has been re-elected president of the Escambia County Blood Bank.

Dr. Kenneth A. Morris, Jacksonville, has been appointed chairman of a committee to supervise the operation of the Duval-Brewster School of Nursing, Jacksonville.

Dr. George H. Warren who has been practicing at Perry for 41 years was honored by his fellow townspeople recently with festivities planned "as an expression of the esteem in which Dr. Warren is held by local citizens." A public barbecue terminated the day long program.

Dr. James A. Sewell has returned to his practice at Melbourne after completing a surgical residency at the University Hospital in Baltimore, Maryland.

Dr. Maurice H. Greenhill has been appointed head of the Department of Psychiatry and director of the Psychiatric Institute. He was formerly professor of psychiatry at the University of Maryland School of Medicine.

Dr. C. C. Hillman, executive director of the Jackson Memorial Hospital since 1946, was recently appointed associate dean of the University of Miami School of Medicine.

Dr. James J. Griffitts, associate director, Medical Research Foundation of Dade County, Inc., Miami, was recently elected the president of the American Association of Blood Banks.

GEORGIA

Dr. John R. Fair has been appointed assistant professor of surgery and Chief of Ophthalmology at the Medical College of Georgia.

Dr. J. Morgan Kellum, Thomaston, was made a qualified Fellow of the International College of Surgeons at the annual meeting that was held in Philadelphia recently. Dr. Kellum is also a Fellow of the American College of Surgeons.

Dr. Daniel C. Elkin, professor emeritus of surgery and former head of the Department of Surgery at Emory University, has been named president-elect of the American College of Surgeons.

Dr. J. Elliott Scarborough, director of the Winship Clinic, Emory University Hospital, has been elected to the National Board of Directors of the American Cancer Society.

The Fifth District Medical Society has recently elected the following officers: Dr. Chester Morse, Decatur, president, Dr. John Slade, vice-president, Dr. J. G. McDaniel, councilor and Dr. Charles S. Jones, vice-councilor. Dr. J. S. Hilsman continues as secretary-treasurer.

Dr. Eugene B. Ferris, Atlanta, was elected vice-president of the American Heart Association at its annual meeting held in New Orleans late in October. In addition to his new post, Dr. Ferris will continue to serve as chairman of the American Heart Association's Medical Advisory Board of the Council on High Blood Pressure Research. Named to the Board of Directors of the Heart Association were Drs. Bruce Logue, Carter Smith and Arthur J. Merrill all of Atlanta.

Dr. G. Darrell Ayer, Jr., Atlanta, was named to the executive committee of the American Society of Clinical Pathologists at the annual meeting held recently in Chicago.

Dr. Lamar B. Peacock, Atlanta, is the newly appointed director of the medical branch, Atlanta Metropolitan Area's Civil Defense Organization.

Dr. Richard Boger was recently elected president of the Greater Atlanta Alumni Association of Duke University and Dr. Sam Ambrose was chosen as one of the vice-presidents.

Drs. F. R. Mann, Frank Mann, Jr., Fred A. Smith, and Duncan B. McRae, McRae, have recently become associated in the practice of medicine as the Telfair Medical Group. Early in September of 1955, the Drs. Mann closed Dr. Mann's Hospital, where they have practiced since 1939.

Dr. Julian Ray Youmans, formerly of Lyons, and Mrs. Youmans are in London, England, where Dr. Youmans will teach and do neurological research at National Hospital of the University of London for nine months.

Dr. M. B. Bowman, Albany, has been made a Fellow of the International College of Surgeons.

Dr. A. Ralph Monaco, Columbus, announces the opening of his private laboratory, "The Monaco Laboratory," with practice limited to clinical labora-

tory procedures, pathology and cytology.

Dr. V. H. Bennett, Gay has been named Meriwether County Physician, taking the place made vacant by the death of Dr. R. B. Gilbert.

Dr. C. E. Irwin, who has been associated with the Warm Springs Foundation since July 1, 1933, and Mrs. Irwin were honored at a farewell party given by employees of the Foundation recently. Dr. Irwin, an orthopedic surgeon, has entered private practice in Atlanta.

Dr. Tofey G. Smaha, Griffin, was made a qualified Fellow of the International College of Surgeons at their recent meeting held in Philadelphia.

Dr. and Mrs. James N. Brawner, Jr., Atlanta, were hosts at a dinner honoring officers, and their wives, of the Southern Psychiatric Association when that association met in Atlanta recently. Dr. and Mrs. Raymond S. Crispell entertained at their home at a breakfast in their honor also.

Dr. C. E. Hall, Atlanta, became Georgia's sixth life master in the Southern Conference Regional Bridge Tournament held recently in Chattanooga. With Mrs. Gertrude Smith, also of Atlanta, as a partner, Dr. Hall won first place in the mixed pairs play.

Dr. L. Harvey Hamff, Atlanta, has been appointed to serve on the national committee on detection and education of the American Diabetic Association.

Dr. Lamont Henry, Atlanta, is the new president of the Georgia Heart Association; he succeeds Dr. Ellison R. Cook, III, Savannah, in that office.

Dr. John R. Lewis, Jr., Atlanta, has been invited to join the Writers Club of Atlanta. Dr. Lewis is a native of Louisville, Kentucky.

Dr. Vernon Skiles, Jr., Atlanta, has been made a Fellow of the International College of Surgeons.

Dr. Joseph S. Skobba, Atlanta, is one of the two new vice-presidents of the Southern Psychiatric Association installed recently.

Dr. Marvin L. Greene, Monticello, has returned from a doctors' tour of Europe. He visited Portugal, Spain, Italy, France, England, Germany, and Austria, where he attended the World Medical Congress.

Dr. R. L. Benson, a native of Marietta, has assumed the duties of Commissioner of Health for the Whitfield-Murray Health Department. He fills the vacancy created last March by the death of Dr. D. L. Butterfield.

Dr. Floyd W. Morgan, Douglasville, has been appointed by the director of the State Crime Laboratory and the director of Public Health to serve as medical examiner for Douglas County.

LOUISIANA

Dr. Alton Ochsner, the William Henderson Professor of Surgery, Tulane School of Medicine, received a distinguished service award from Louisiana College, Pineville, Louisiana. Dr. Ochsner received the award on October 6, when the college celebrated its 49th birthday.

Dr. Ralph M. Hartwell, director, Pathology Department, Hotel Dieu, New Orleans, was elected vice-president of the American Association of Blood Banks at the eighth annual meeting of the association held in Chicago in November.

Dr. A. J. Warren, former director of the Rockefeller Foundation's division of medicine and public health delivered the principal address during the dedication of the new 10-story addition to Hutchinson Memorial Medical building of the Tulane School of Medicine. During the ceremonies, Dr. Warren was awarded an honorary doctor of law degree for his outstanding services in the fields of medicine and public health.

New appointments in the Tulane University School of Medicine are: Drs. Loraine Friedman, assistant professor of microbiology, C. E. Clark, instructor in ophthalmology, C. L. M. Samson, instructor in ophthalmology, Henry C. Pitot, Friedrichs H. Harris and Samuel French, instructors in pathology; Joseph Schramel, instructor in surgery; Adele E. Edison, instructor in psychiatry; James F. Van Pelt, Jr., instructor in obstetrics and gynecology; Cyril Y. Bowers, instructor in medicine; Isadore Yager, instructor in medicine; Richard Hibbs, instructor in anatomy; William G. Palfrey, instructor in pediatrics; Ambrose Hampton, instructor in medicine and tropical medicine; Gustave Kuehnle, instructor in otolaryngology.

Dr. William W. Frye, dean, and Dr. Henry E. Meleney, research professor of medicine of the Louisiana State University School of Medicine, New Orleans, attended the meetings of the American Society of Tropical Medicine and Hygiene in Boston in November. Dr. Meleney gave a report on the China Medical Board Fellowship Program for Teachers of Parasitology and Tropical Medicine. From Boston Dr. Frye went directly overseas for the beginning of a three months, round the world trip during which he will lecture and review the work in tropical medicine and parasitology laboratories in 18 countries.

Dr. James T. Nix, Jr., clinical instructor in surgery, Louisiana State University School of Medicine, New Orleans, was inducted as president of the American College of Gastroenterology at their meeting in Chicago on October 21.

Dr. F. Theo Beatrous, New Orleans, was certified by the American Board of Otolaryngology at a meeting of the board in Chicago recently.

Dr. George S. Ellis, New Orleans, was recently certified by the American Board of Ophthalmology.

Dr. Vincent P. Blandino, New Orleans, was elected president of the Louisiana Academy of General Practice at the ninth annual scientific assembly in Shreveport on October 14-16.

Dr. Emma S. Moss, New Orleans, took office as president of the American Society of Clinical Pathologists at the group's thirty-fourth annual meeting in Chicago recently.

MARYLAND

Dr. W. Raymond McKenzie, Baltimore, was elevated to the presidency of the Southern Medical Association during the 1955 annual meeting in Houston, Texas, November 14-17. The installation ceremonies took place during the business session of the annual dinner-dance sponsored by the Association on Wednesday evening, November 16.

Dr. Samuel P. Bessman, director of biochemical research of the Research Foundation at Children's Hospital, Washington, D. C., has been appointed associate professor of pediatrics in the University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore.

Dr. Harold Rosen, Baltimore, has been elected

Continued on page 34

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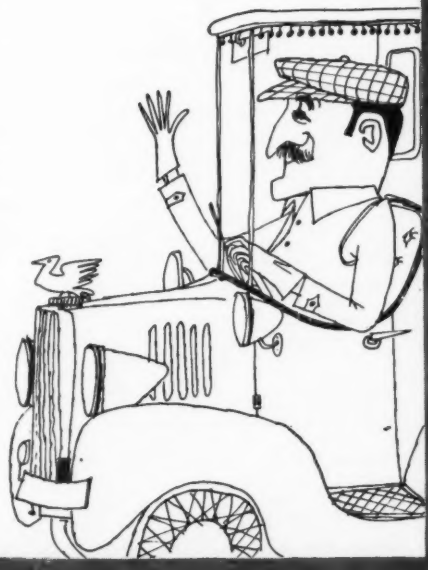

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MEDICAL HORIZONS TV Monday P.M. Sponsored by CIBA ABC-TV

Continued from page 100

executive secretary of the Society for Clinical and Experimental Hypnosis.

MISSISSIPPI

Dr. J. P. Culpepper, Jr., Hattiesburg, is the new president-elect of the Southern Medical Association. Dr. Culpepper was elected to his new office during the Association's recent annual meeting held in Houston, Texas, last November 14-17.

The full-time clinical faculty of the new University of Mississippi Medical Center in Jackson are as follows: Department of Medicine: Dr. J. R. Snavely, professor and chairman; Dr. Warren Bell, associate professor; Dr. Thomas M. Blake, assistant professor and chief of cardiopulmonary section; Dr. Fred Allison, Jr., assistant professor and chief of infectious disease section; Dr. Herbert G. Langford, assistant professor and chief of metabolism and endocrinology. Obstetrics and Gynecology: Dr. Michael Newton, professor and chairman. Pediatrics: Dr. Blair Batson, professor and chairman. Preventive Medicine: Dr. Thomas J. Brooks, Jr., professor and chairman; Dr. Lewis F. Rittelmeyer, associate professor, family practice; Dr. William Hutchinson, assistant professor. Radiology: Dr. Robert Sloan, professor and chairman. Surgery: Dr. James Hardy, professor and chairman; Dr. G. Bittenbender, professor of anesthesiology; Dr. Naomi Dalton, instructor in anesthesiology; Dr. Watts R. Webb, instructor; Dr. Orlando Andy, professor of neurosurgery; Dr. James S. Browne, instructor in neurosurgery; Dr. Don Turner, instructor in surgical research and physiology.

MISSOURI

Dr. Daniel L. Sexton, St. Louis, nationally known internist, is the recipient of the 1955 Distinguished Service Award given by the Mississippi Valley Medical Society. Dr. Sexton is the immediate past second vice-president of the Southern Medical Association.

Dr. Donald Greiff, professor of biology, St. Louis University School of Medicine, has been appointed an associate member of the Commission on Rickettsial Diseases of the Armed Forces Epidemiological Board.

Officers of the Golf Club for the year 1956 at the Norwood Hills Country Club, St. Louis, are as follows: Dr. C. G. Vournas, president, Dr. L. A. Reuter, secretary, Dr. F. G. Weinel, treasurer. The president's trophy held by the president of the Golf Club each year, known as the Reuben M. Smith Memorial Trophy donated by the staff of St. Anthony's Hospital, will be in the possession of the new president, Dr. Vournas.

Dr. Oliver Lowry has recently been named dean of the Washington University School of Medicine. Dr. Lowry has been professor of pharmacology and head of the department since 1947. He succeeds Dr. Carl V. Moore who resigned to devote full time to research and teaching.

The Mid-Continent Psychiatric Association at a meeting in Tulsa, Oklahoma recently elected Dr.

Continued on page 39

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A two months combined course comprising attendance at clinics and lectures; instruction in examination, diagnosis and treatment; pathology, radiology, anatomy, operative proctology on the cadaver, anesthesiology, witnessing operations, examination of patients pre-operatively and post-operatively in the wards and clinics; attendance at departmental and general conferences.

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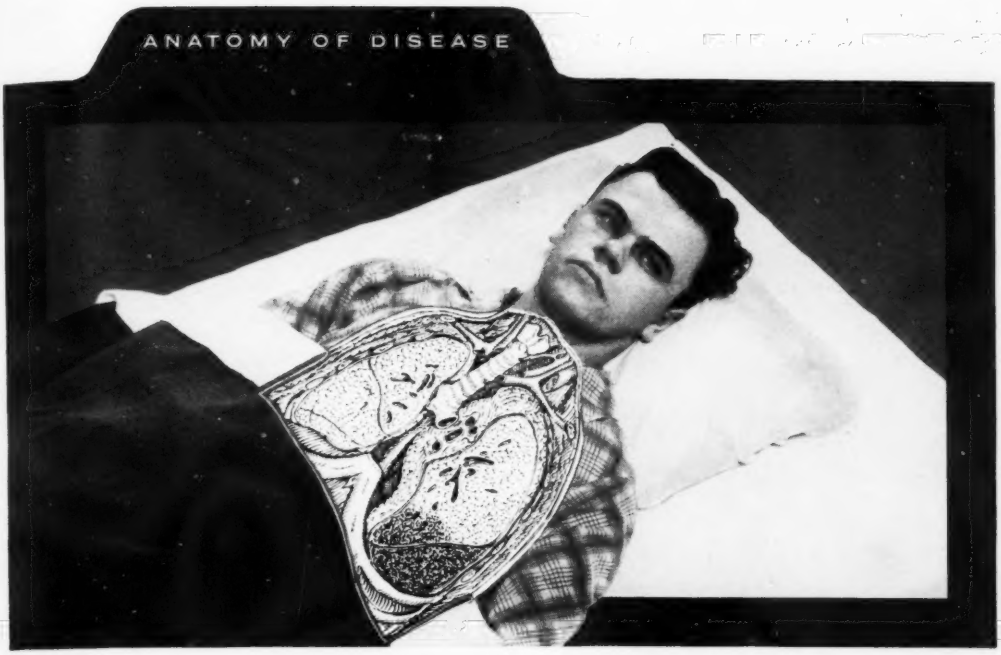

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* *Brit. Med. J. Vol. 11, No. 4839, p. 757, 1953*
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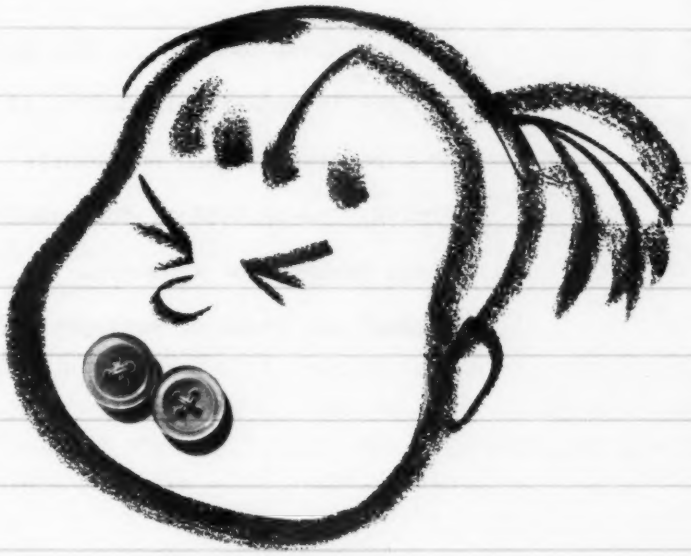

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Progressive brain damage is most frequently associated with arteriosclerosis and capillary fragility often resulting from a variety of causes.

These include long standing hypertension; chronic renal disease whether due to glomerulonephritis, nephrosclerosis, chronic pyelonephritis. In long standing diabetics, this condition is noted in a certain percentage of patients with Kimmelstiel-Wilson Syndrome. Although the primary disease is very different in these various entities, the final pathological findings are remarkably similar, capillary fragility.

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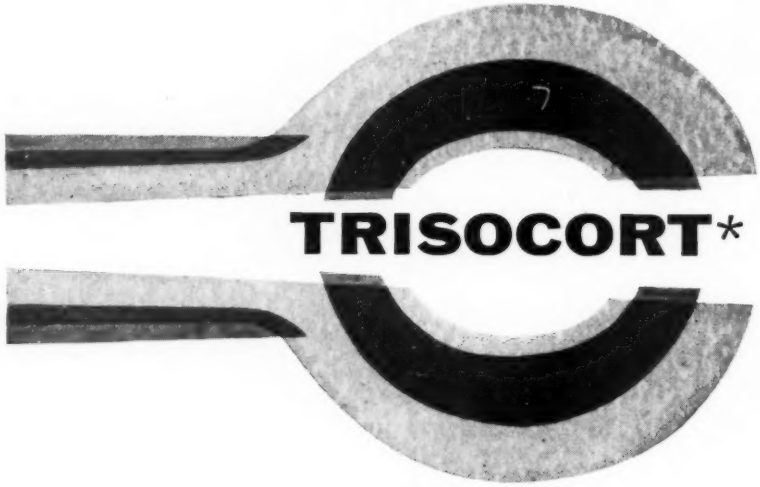

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Continued from page 34

Frank J. Koenig and Dr. Paul Hines, Kansas City, editors of *The Bulletin*.

Dr. A. R. Timerman, St. Joseph, closed his office on October 1 after sixty-one years as a practicing physician. He expects to spend part of his time with a son in Florida.

Dr. Robert E. Bruner, Kansas City, was recently elected chairman of the medical advisory board of the Kansas City United Cerebral Palsy Association.

Dr. Wilbur P. McDonald, St. Joseph, was presented an award recently by the Buchanan County Tuberculosis Society in appreciation for his work with and counsel to the organization for the nine years he has served on the board.

The new staff of Deaconess Hospital, St. Louis, are the following: Dr. Clarence E. Mueller, St. Louis, president, Dr. Edward M. Cannon, St. Louis, vice-president, and Dr. Birkle Eck, secretary-treasurer.

Dr. William H. Olmsted, St. Louis, has been re-appointed vice-chairman of the National Committee on Diabetes Detection and Education of the American Diabetes Association.

The Buchanan County Unit of the American Cancer Society recently elected Dr. H. Sheffield Jeck, Jr., St. Joseph, president. Serving on the board are Drs. Joseph O. Fisher, Thompson E. Potter, H. Ewing Wachter and Henry C. Willumsen, St. Joseph.

Dr. W. O. Finney was recently presented a trophy

Continued on page 40

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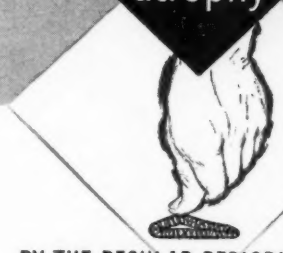
The Tucker Hospital is for the treatment of nervous and endocrine diseases. There are departments of massage, medicinal exercises, hydrotherapy and physiotherapy. The Hospital is large and bright, surrounded by a lawn and shady walks, large veranda and has a roof garden. It is situated in the best part of Richmond and is thoroughly and modernly equipped. The nurses are specially trained in the care of nervous cases.

IN CORTICOID-TREATED PATIENTS

minimize adrenal suppression and atrophy



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b. 100 U. of HP*ACTHAR *Gel* for every 200 to 300 mg. of hydrocortisone.

c. 100 U. of HP*ACTHAR *Gel* for every 400 mg. of cortisone.

2 Discontinue use of steroid on the day of injection.

*Highly Purified. HP*ACTHAR *Gel* is The Armour Laboratories brand of purified corticotropin.

THE ARMOUR LABORATORIES

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Continued from page 39

as the City of Chaffee's outstanding citizen for his civic and professional contribution to the community. Dr. Finney has practiced medicine in Chaffee since 1910.

NORTH CAROLINA

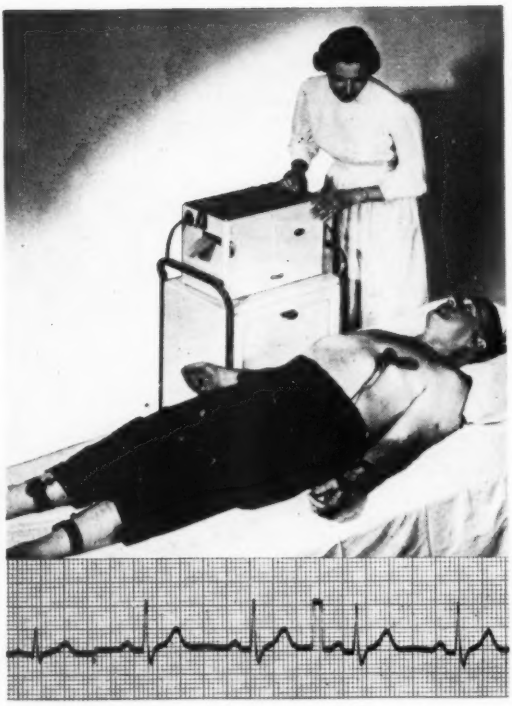
Dr. A. T. Miller, professor of physiology, University of North Carolina School of Medicine, attended a teaching symposium on the Basic Sciences in Aviation Medicine, at the School of Aviation Medicine, Randolph Field, Texas, recently. This was the first of a projected series of symposia on the role of the medical schools in training future physicians in those aspects of medicine essential for national defense. These symposia are sponsored by the Medical Education for National Defense program, in which some 15 medical schools are currently participating.

Dr. Christopher T. Bever and Dr. Lucie Jessner, Department of Psychiatry, University of North Carolina, are currently teaching at the Washington Psychoanalytic Institute on a part-time basis.

Dr. Bayard Carter, Duke University physician, has been named president of the American Board of Obstetrics and Gynecology.

The North Carolina Surgical Association has elected the following officers: Dr. Edward W. Phifer, Morganton, president, Dr. Alexander Webb, Raleigh, president-elect, Dr. Howard Starling, Winston-Salem, vice-

Continued on page 42



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Packages: 2 cc. vial (1 immunization)
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- Rauwiloid represents the balanced, mutually potentiated actions[1] of several Rauwolfia alkaloids, of which reserpine and the equally antihypertensive rescinnamine have been isolated.
- Hence, reserpine is not the total active antihypertensive principle of the rauwolfia plant.
- Rauwiloid, the alseroxylon fraction of Rauwolfia serpentina, Benth., is freed of the undesirable alkaloids of the whole root. Recent investigations confirm the desirability of Rauwiloid (because of the balanced action of its contained alkaloids) over single alkaloidal preparations; "...mental depression...was...less frequent with alseroxylon..."[2]

The dose-response curve of Rauwiloid is flat, and its dosage is uncomplicated and easy to prescribe... merely two 2mg. tablets at bedtime.

1. Cronheim, G., and Toekes, I.M.: Comparison of Sedative Properties of Single Alkaloids of Rauwolfia and Their Mixtures, Meeting of the American Society for Pharmacology and Experimental Therapeutics, Iowa City, Iowa, Sept. 5, 1955.

2. Moyer, J.H.; Dennis, E., and Ford, R.: Drug Therapy (Rauwolfia) of Hypertension. II. A Comparative Study of Different Extracts of Rauwolfia When Each Is Used Alone (Orally) for Therapy of Ambulatory Patients with Hypertension, A.M.A. Arch. Int. Med. 96:530 (Oct.) 1955.

Riker

LOS ANGELES

Rauwiloid is the original alseroxylon fraction of India-grown Rauwolfia serpentina, Benth., a Riker research development.

Continued from page 40

president, and Dr. Alfred Hamilton, Raleigh, secretary-treasurer.

The Sixth District Medical Society at a recent business session approved the following slate of new officers: Dr. L. E. Fields, Chapel Hill, president, Dr. Lillard F. Hart, Apex, vice-president, Dr. Seth G. Hobart, Durham, secretary-treasurer.

OKLAHOMA

Dr. Harry Dale Murdock, veteran Tulsa surgeon, was presented a gold 50-Year Club pin by the Oklahoma State Medical Association. The presentation was made at a recent meeting of the Tulsa County Medical Society.

Dr. J. E. Cochrane, Byars, was honored recently at a surprise party given by 500 of his friends honoring his 38 years of medical practice.

Dr. Onis Franklin, Broken Arrow, was honored with a Dr. Franklin Day in that city recently.

Dr. A. C. Fina has been named chief of the staff of Mary Hurley Hospital in Coalgate.

Dr. Frank J. Nelson, Tulsa, has been named head of the health division of the Tulsa Council of Social Agencies.

Dr. W. B. Lain, Clinton, has joined the Carnegie Hospital staff.

Dr. J. L. Cox, Ardmore, was honored recently by the University of Tennessee at their "Golden T" ceremonies.

Dr. C. W. Tedrowe, Woodward, was honored recently as the oldest living former grand High Priest in northwestern Oklahoma by more than one hundred Masons from that region who gathered in Woodward.

SOUTH CAROLINA

Dr. Robert Wilson, Charleston, has been appointed chairman of the Roper Hospital Expansion Committee to replace Dr. Robert Hope who requested to be relieved of the chairmanship.

The Pilot Club of Abbeville presented a $500 check and bronze door plaque to Abbeville County Memorial Hospital in honor of the late Abbeville physician-brothers, Dr. John Rayford Power and Dr. Eugene Logan Power. A room in the hospital's new wing was dedicated in their honor.

Dr. Julian P. Price, Florence, was presented a silver cup honoring him upon his retirement as dean of the Southern Pediatric Seminar at Saluda. Dr. Warren Quillian of Coral Gables, Florida, made the presentation.

Dr. Jack C. Scurry has rejoined the staff of Scurry Clinic after a year's absence on a postgraduate study fellowship at Memorial Hospital in New York City.

Dr. Mauldin J. Boggs, for 16 years an outstanding physician in Abbeville, is leaving to enter the Postgraduate Division of the Tulane University School of Medicine at New Orleans for a proposed two year study course.

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1-oz. Bottle with Dropper

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'Propadrine' Hydrochloride . .3%
(Phenylpropanolamine Hydrochloride)
Phenylephrine Hydrochloride .15%
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★ No Bad Taste
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and for **Convenience**

½-oz. Plastic Spray Bottle
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Ethical Specialties for the Profession

RHINALL Cold Capsules
RHINAMIN CAPSULES in Allergic Colds
PYROCAIN in Acute Otitis Media

Dr. Lawson Hamilton Bowling, Jr. assumed his duties as clinical director of the Columbia division, South Carolina State Hospital on August 1.

Dr. Sol B. McLendon has had the dual position of clinical director of both the Columbia and the State Park Divisions since September 1952. His entire time will now be devoted to State Park where the patients number approximately one-half of the total patient population of 6,062.

TENNESSEE

Dr. John B. Youmans, Nashville, was elected president-elect of the Association of American Medical Colleges at its annual meeting recently. Dr. Youmans had been treasurer of the organization for a number of years.

Four new staff members have been added to the University of Tennessee College of Medicine, Division of Chemistry. They are: Drs. Robert L. Fischer, William E. Jefferson and Frederick W. Lengemann as instructors and Dr. Martin Loyd Minthorn, Jr., as research associate. Dr. Robert C. Rendtorff has joined the staff as assistant professor of preventive medicine.

Dr. Ira S. Pierce, Jr., Knoxville, has recently been employed as the Knox County physician.

Dr. Joe Strayhorn, Nashville, is chairman of the Accident Prevention Committee for Tennessee of the American Academy of Pediatrics.

Continued on page 47

CITY VIEW

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- minimizes sodium retention edema
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in **rheumatoid arthritis:** better relief of pain, swelling, tenderness; diminishes joint stiffness

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Continued from page 43

Dr. N. H. Culbertson, Chapel Hill, was recently honored by his townspeople on his seventy-second birthday.

Dr. J. H. Gammon, Knoxville, has been employed by the Knox County Commission.

Dr. John C. Burch, Nashville, has been named president of the Nashville-Davidson County Chapter, American Cancer Society. Dr. B. F. Byrd, Jr., Nashville, has been named vice-president.

Dr. John C. Sharp, Etowah, has been elected a member of the McMinn County Council.

The Nashville Obstetric and Gynecological Society has elected Dr. D. Scott Bayer, Nashville, president, Dr. R. E. Wyatt, Jr., vice-president, Dr. Homer M. Pace, secretary, and Dr. Russell T. Birmingham, treasurer.

The University of Tennessee Medical Unit honored Dr. I. H. Beasley, Gallatin, Dr. G. G. Keener, Kingsport, Dr. Edward Deal Gross, Chestnut Mound, and Dr. Basil Mayo at the recent commencement exercises.

TEXAS

The American Association of Blood Banks held their eighth annual meeting in Chicago, November 19-21. Dr. E. E. Muirhead was elected president-elect. Dr. Muirhead is professor of pathology and chairman of the department of the University of Texas Southwestern Medical School, Dallas, and chief, Depart-

Continued on page 50

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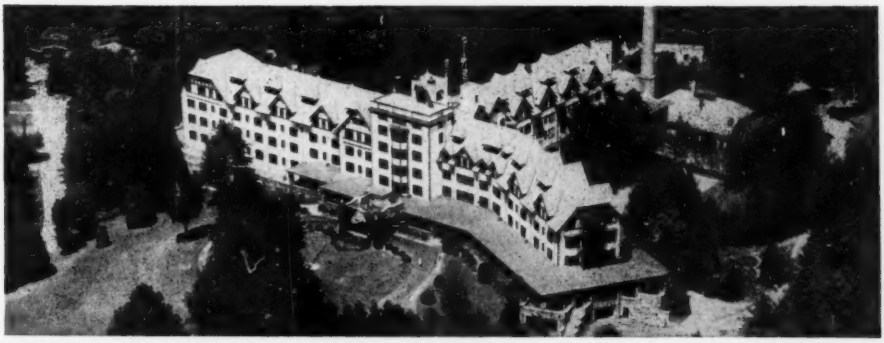

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Dr. Rudolf J. Noer	Louisville, Ky.	Surgery
Dr. Frank Glenn	New York, N. Y.	Surgery
Dr. Kenneth Pickrell	Durham, N. C.	Surgery
Dr. Henry G. Schwartz	St. Louis, Mo.	Neurosurgery
Dr. Arthur Grollman	Dallas, Texas	Medicine
Dr. T. S. Danowski	Pittsburgh, Pa.	Medicine
Dr. Albert Segaloff	New Orleans, La.	Medicine
Dr. B. Y. Glassberg	St. Louis, Mo.	Medicine
Dr. C. P. Rhoads	New York, N. Y.	Pathology
Dr. George L. Sackett	Cleveland, Ohio	X-Ray
Dr. Warren E. Wheeler	Columbus, Ohio	Pediatrics
Dr. Harry Bakwin	New York, N. Y.	Pediatrics
Dr. John C. Ullery	Columbus, Ohio	Obstetrics & Gynecology
Dr. Edward D. Allen	Chicago, Ill.	Obstetrics & Gynecology
Dr. Alson E. Braley	Iowa City, Iowa	Ophthalmology
Dr. David E. S. Wishart	Toronto, Canada	Ent
Dr. William M. Coppridge	Durham, N. C.	Urology
Dr. William H. Bickel	Rochester, Minn.	Orthopaedic Surgery

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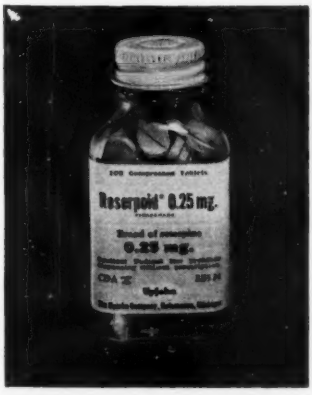

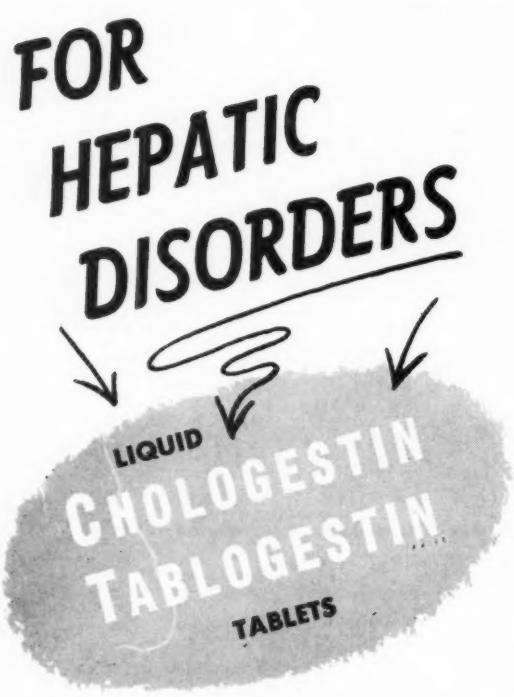

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DR.....

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Continued from page 47

ment of Pathology, Parkland Memorial Hospital, also in Dallas.

The International College of Surgeons has recently elected to fellowship Dr. Harvey Renger, Hallettsville, and Perry J. C. Byars, Jr., San Angelo.

Dr. A. L. Thomas, Ennis, has been elected to membership in the American Academy of General Practice.

The World Medical Association meeting in Vienna, Austria was attended by the following physicians: Dr. C. B. Gardner, Merkel, Dr. Joseph F. McVeigh and Dr. W. M. Crawford, Fort Worth.

Dr. Charles M. Henner has resigned his position as mayor of Santa Anna and has gone to Trinidad, British West Indies, as a medical missionary. He will be chief of surgeons at the Port of Spain Adventist Clinic.

Dr. Gladys J. Fashena, professor of pediatrics at Southwestern Medical School of the University of Texas, Dallas, has been re-elected to another five year term on the board of governors of Playtex Park Research Institute, the pediatric research foundation of Dover, Delaware.

Dr. Frank J. McGurl, Houston, is a new member of the executive council of the Association of Life Insurance Medical Directors of America.

Dr. W. L. Crosthwait, Waco, has neared completion of his autobiography, "The Last Stitch," which will be published by the J. B. Lippincott Company this year.

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DIVISION OF GRADUATE MEDICINE

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Pediatric Neurology — Feb. 27-March 3, 1956

Industrial Medicine — Apr. 12-13, 1956

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Dr. A. W. Cowin, Dalhart, has sent more than $6,000 worth of medical equipment to South Korea through the American-Korean Foundation.

Dr. R. R. Wills, Hereford, has been elected to the board of directors of the Commonwealth Credit Corporation, Houston.

The Texas Surgical Society has elected the following new officers for the coming year: Dr. P. I. Nixon, Sr., San Antonio, president, Dr. J. E. Dailey, Houston, first vice-president, Dr. Hub E. Isaacks, Fort Worth, second vice-president, Dr. Robert L. Sewell, Fort Worth, treasurer, and Dr. Albert W. Hartman, Jr., San Antonio, secretary. Dr. John Warner Duckett, Dallas, was elected a member of the council to succeed Dr. Frank A. Selecman, whose term expired.

New officers of the Texas Academy of General Practice are Dr. James D. Murphy, Fort Worth, president, Dr. George V. Launey, Dallas, president-elect, Dr. Cecil M. French, San Angelo, vice-president, Dr. John M. Smith, Jr., San Antonio, treasurer, and Dr. Carlos Fuste, Alvin, delegate to the American Academy of General Practice.

Dr. Stephen R. Lewis is the new director of the Postgraduate Division of the University of Texas Medical Branch, Galveston. Dr. Lewis is taking the position formerly held by Dr. E. Ivan Bruce.

VIRGINIA

The Neuropsychiatric Society of Virginia has recently elected the following officers: Dr. R. W. Garnett, Jr., Charlottesville, president, Dr. George S. Fultz, Jr., Richmond, vice-president, Dr. Thomas F. Coates, Jr., Richmond, secretary-treasurer. Drs. W. D. Buston, Charlottesville, and Howard R. Masters, Richmond, were named to the executive committee.

Dr. Charles L. Outland, director of the Richmond Public Schools Medical Department, has been granted a three month leave of absence for a United Nations mission to Iraq. He accepted an invitation from the World Health Organization to help set up a government school health program in Iraq.

Dr. Walter B. Martin, Norfolk, was one of the official four-man delegation to the ninth General Assembly to the World Medical Association in Vienna, Austria, recently.

Dr. Walter E. Vermilya, Clifton Forge, has been elected to the presidency of the Little Theatre Group.

Dr. Margaret Glendy, Roanoke, has been named "Woman of the Year" by the Business and Professional Woman's Club.

Dr. A. I. Dodson, Richmond, presented three papers before the sixth annual meeting of the Puerto Rico Urological Association at San Juan recently.

Dr. Benjamin W. Rawles, Jr. has been elected president of the Richmond Chapter of the American Red Cross. Among the new board members are Drs. Gordon D. Hall, Thomas N. P. Johns, and John R. Massie, Jr.

Dr. H. D. Crow has been appointed as director of the State Health Department's new medical train-

Continued on page 54

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COMPLEX

assures full potency

Separate packaging of dry vitamins and diluent (mixed immediately before injection) assures the patient a more effective dose. May also be added to standard IV solutions.

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Each 2 cc. dose contains:

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Pyridoxine HCl (B_6)	5 mg.
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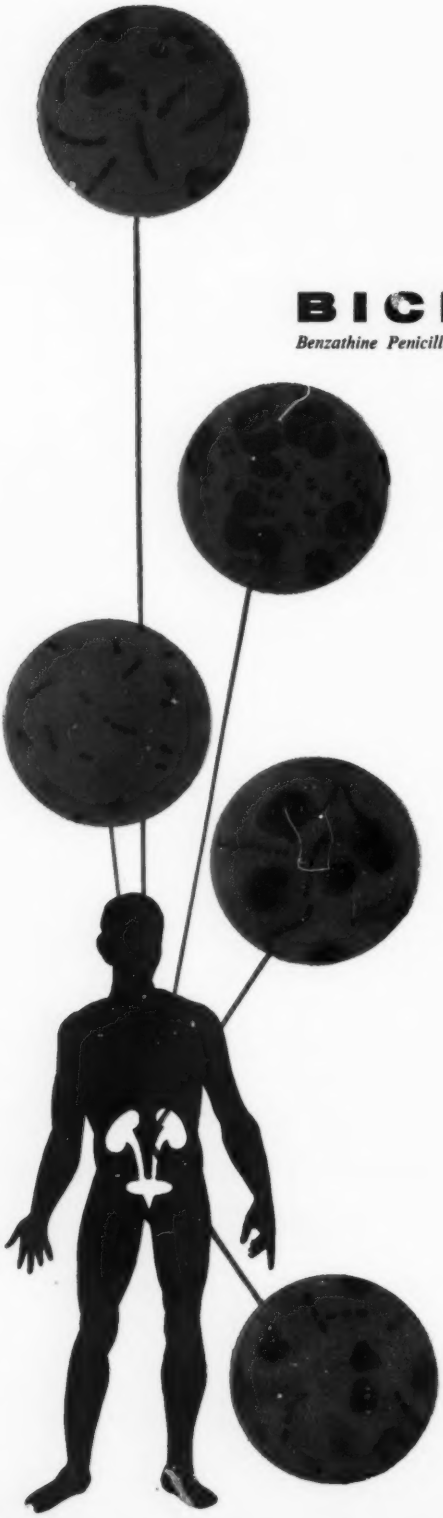

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*Suspension only

1. Spink, W.W.: J.A.M.A. *152:585* (June 13) 1953
2. Bush, W.L.: Southern M. J. *45*:870 (Sept.) 1952
3. Berkowitz, D.: Antibiot. & Chemo. *3*:618 (June) 1953.

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PABALATE — Each yellow enteric coated tablet contains sodium salicylate U. S. P. 0.3 Gm. (5 gr.), sodium para-aminobenzoate 0.3 Gm. (5 gr.), and ascorbic acid 50 mg.

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stimulates secretion of corticotropin ... prolongs action of endogenous corticosteroids

free from adverse reactions.

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NOW—effective **Steroid Hormone**

therapy of rheumatic affections with

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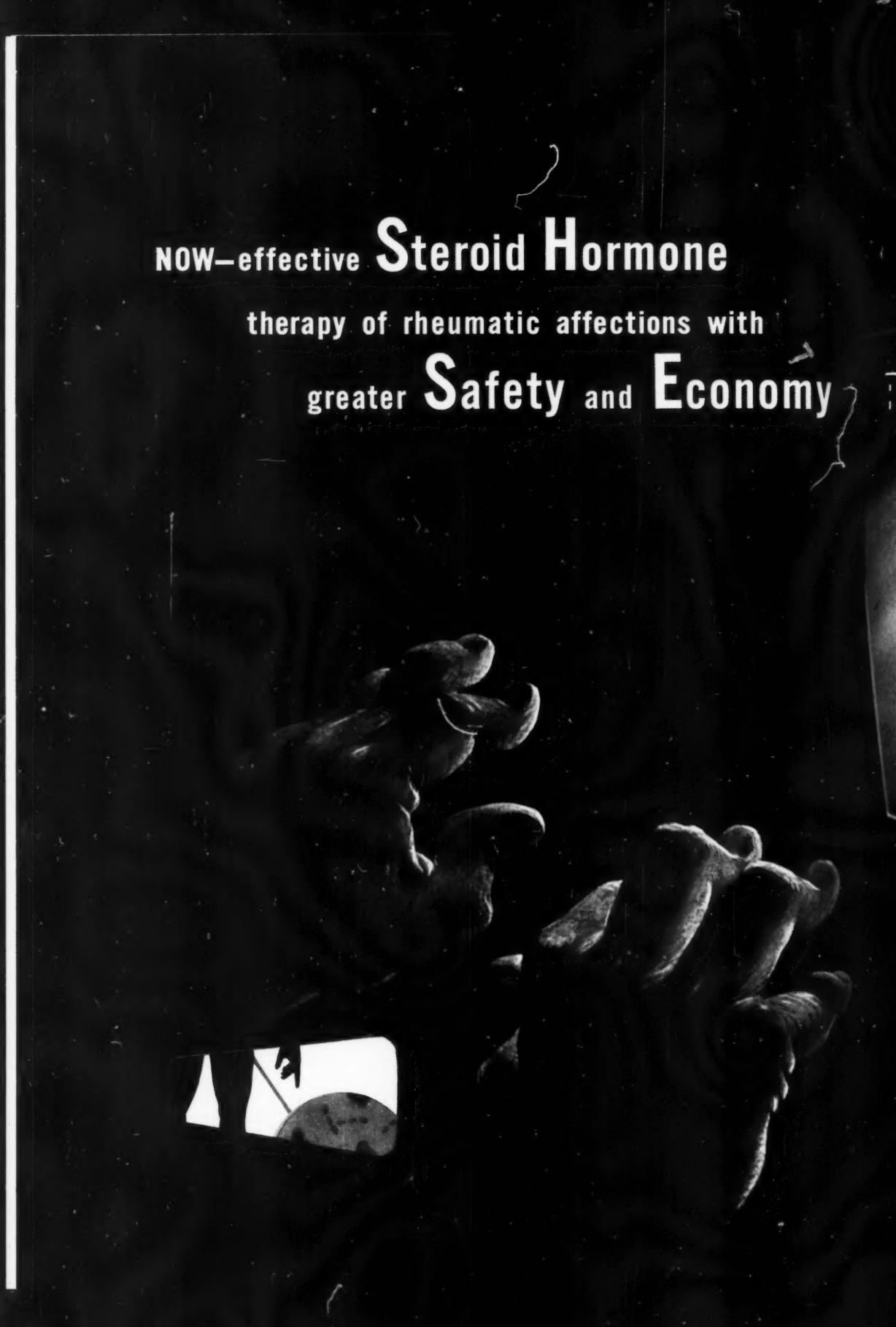

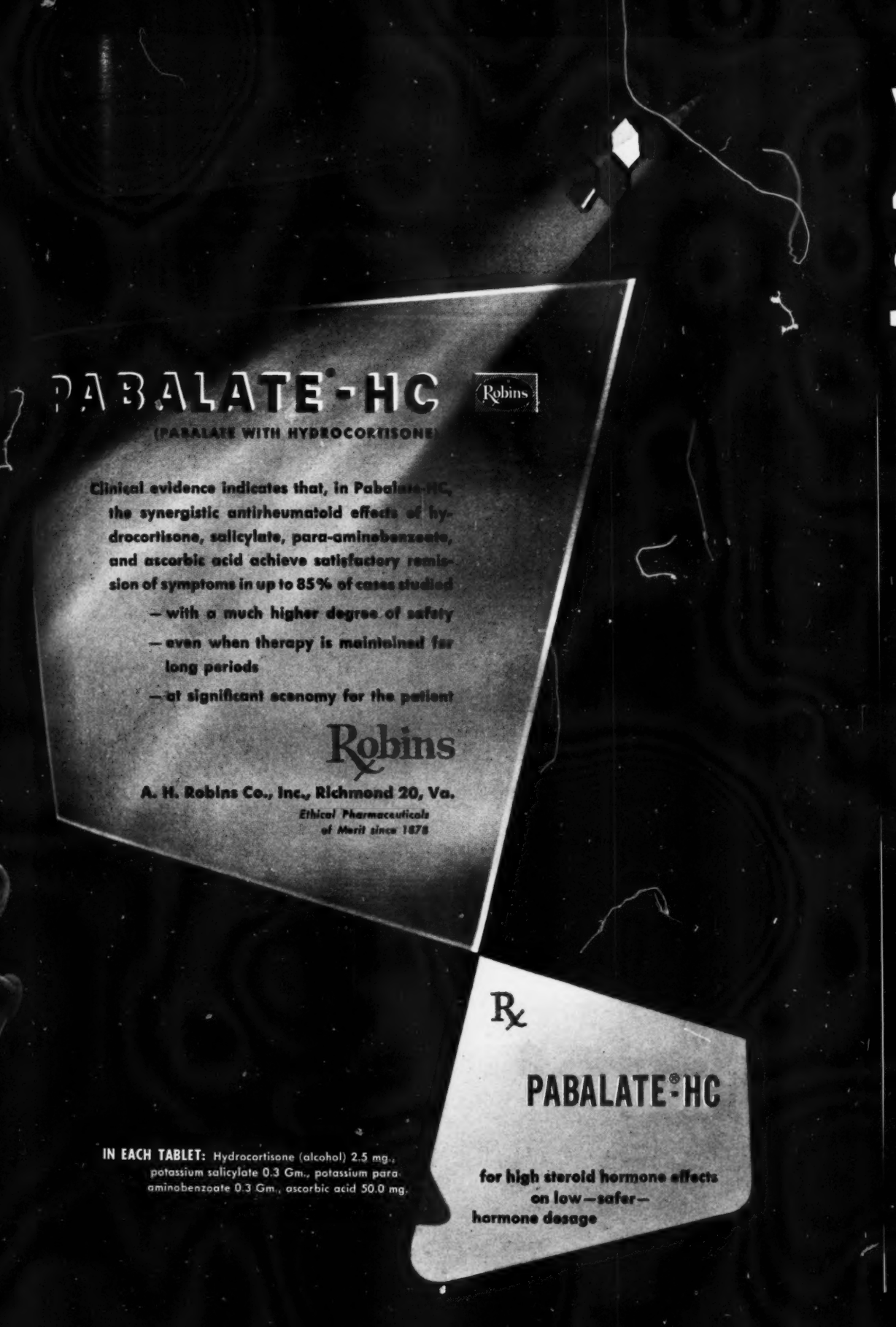
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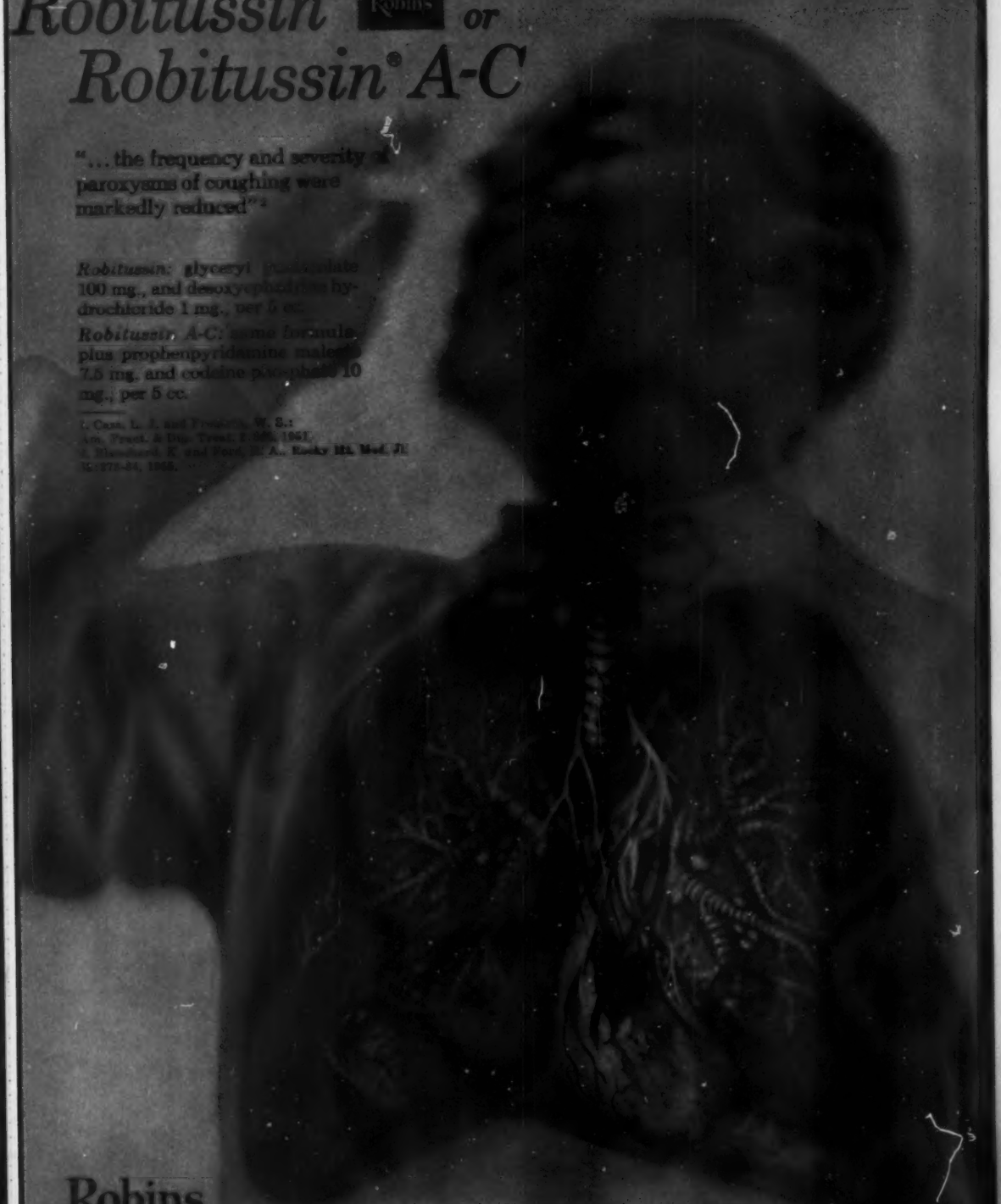
1. Cass, L. J. and Frederick, W. S.: Am. Pract. & Dig. Treat. 5:569, 1954.
2. Blanchard, E. and Ford, [illegible] A., Rocky Mt. Med. J. 55:878-84, 1958.



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Pontocaine® hydrochloride	10 mg.
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— in a cacao butter base —

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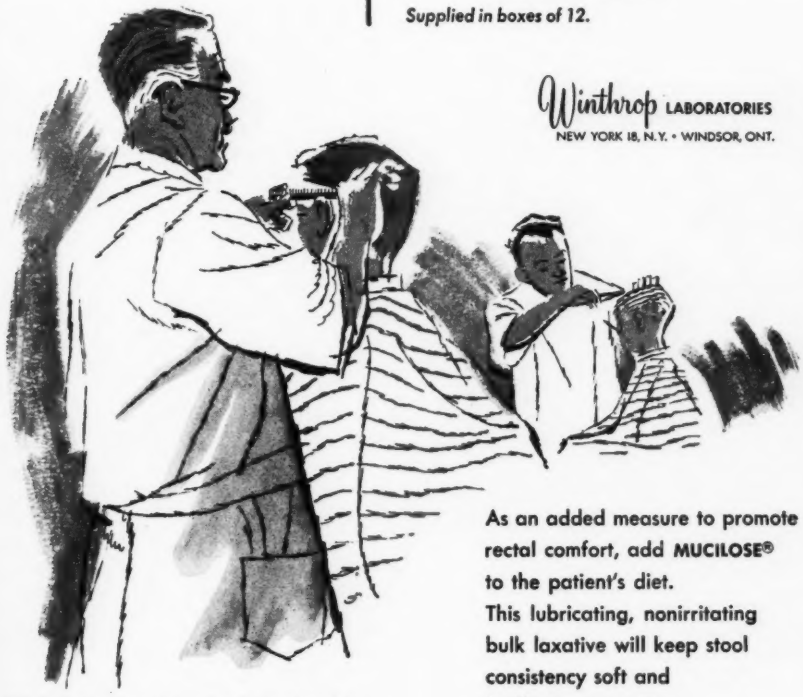

As an added measure to promote rectal comfort, add **MUCILOSE®** to the patient's diet. This lubricating, nonirritating bulk laxative will keep stool consistency soft and facilitate evacuation.

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1. McLester and Darby: "Nutrition and Diet in Health and Disease," ed. 6, Saunders, p. 195. 2. McCay, C. M., in Lansing: "Problems of Aging," ed. 3, Williams and Wilkins, 1952, p. 193. 3. Sebrell and Hundley, in Stieglitz: "Geriatric Medicine," ed 3, Lippincott, 1954, p. 189.

Continued from page 51

ing section. He will also hold the position of director for the health district of Suffolk and the counties of Southampton, Isle of Wight and Nansemond, with his headquarters at Suffolk.

Dr. John Williams Powell, Richmond, has been named medical director of the Chesapeake and Potomac Telephone Company.

Dr. Lewis A. Micou, Buena Vista, was elected medical advisor of the Virginia Association of Rescue Squads at the group's recent annual meeting.

Dr. W. T. Sanger will be given a newly created post of chancellor at the Medical College of Virginia next July 1. This post was created due to his compulsory retirement from the presidency at the age of 70. Dr. Sanger will assist in planning further development of the college and will act in an advisory capacity. Dr. R. Blackwell Smith, Jr., dean of the School of Pharmacy, will become president of the college. He has been serving as assistant president since last March.

Dr. James H. Roberts, Roanoke, has been awarded a certificate of merit and pin by the National Medical Association in recognition of the forty or more years of valuable service he has rendered to the citizens of his state, the nation and the Association.

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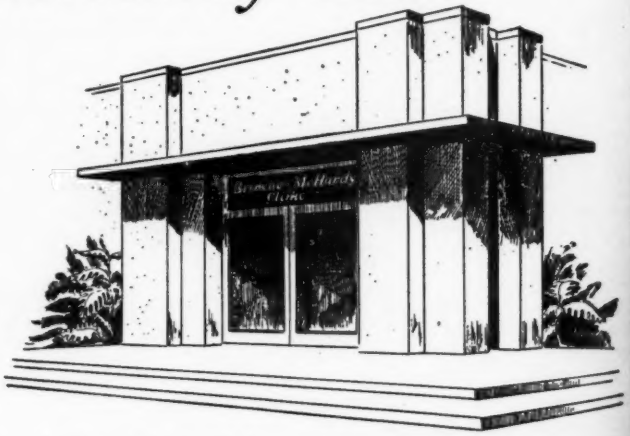

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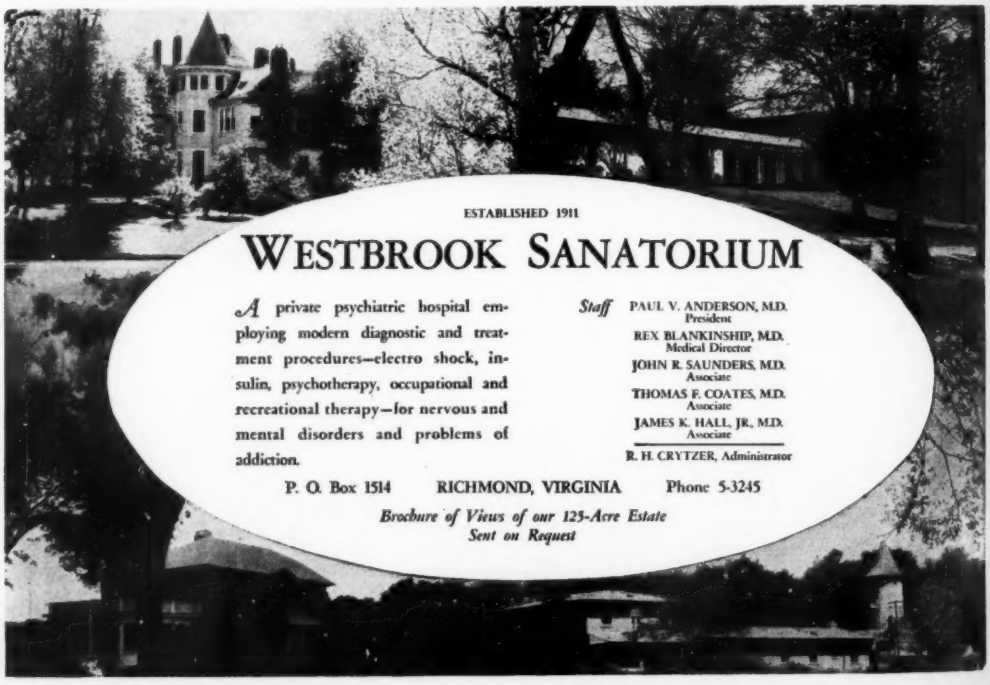

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REFERENCES:

1. Coles, B. L.: Arch. Disease in Childhood *30*:121 (April) 1955.
2. Weinsaft, P. P., and Bernstein, L. H. T.: Amer. J. Med. Sc. *230*:264 (Sept.) 1955.
3. Vilter, R. W.: Amer. J. Clin. Nutr. *3*:72 (Jan.-Feb.) 1955.
4. Cartwright, G. E.: Amer. J. Clin Nutr. *3*:11 (Jan.-Feb.) 1955.

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- 89.9% cure rate, shown in 4 clinical studies*, 108 cases, including many which were refractory to previous therapy. Results in *one menstrual cycle* plus a few days, with this dual treatment method. Few recurrences, demonstrated by repeated microscopic examinations
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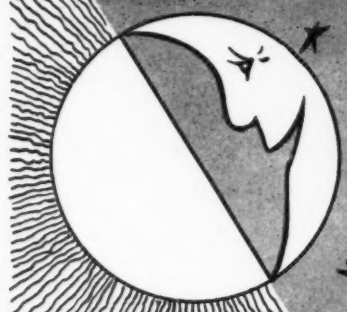

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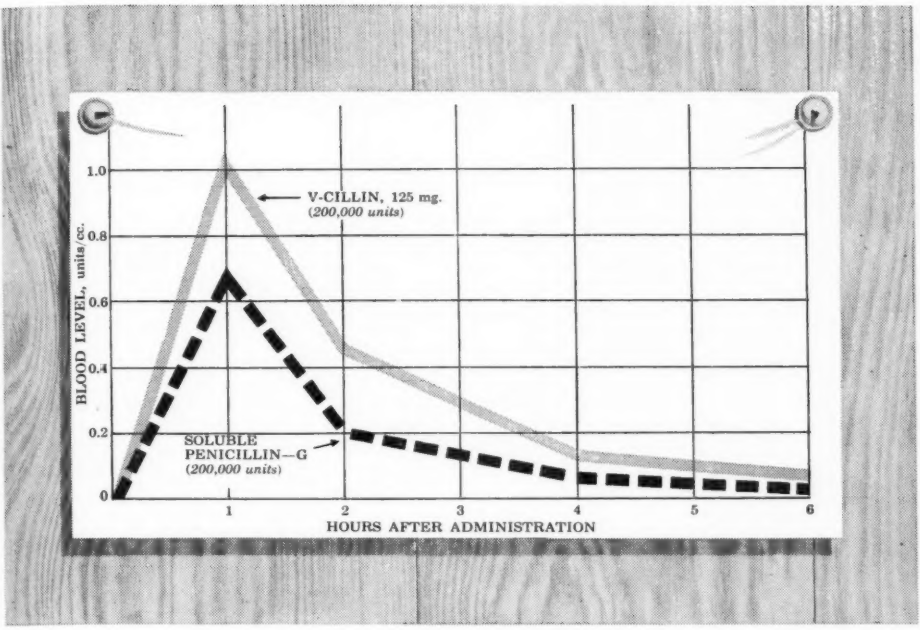

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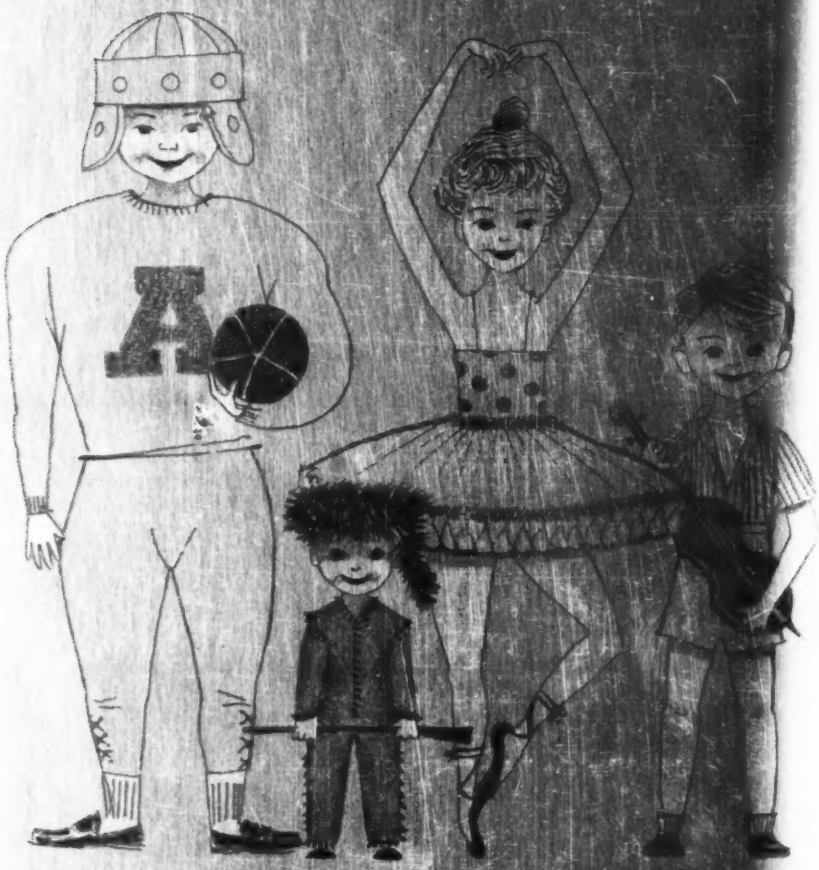

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